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=> fil hcaplus
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FILE COVERS 1907 - 7 Sep 2005  VOL 143 ISS 11
FILE LAST UPDATED: 6 Sep 2005  (20050906/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

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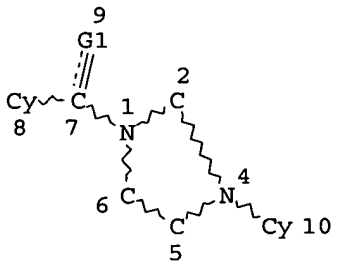


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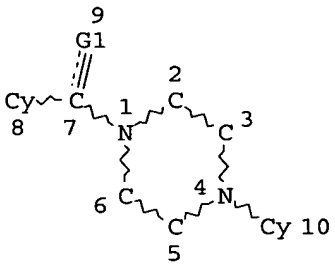

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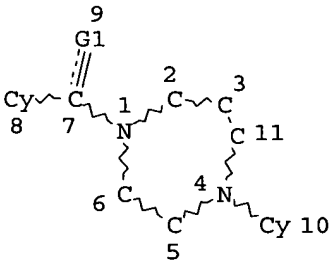

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STEREO ATTRIBUTES: NONE
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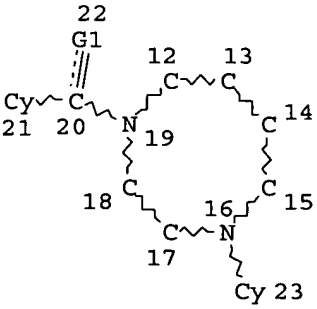

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DEFAULT MLEVEL IS ATOM
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STEREO ATTRIBUTES: NONE
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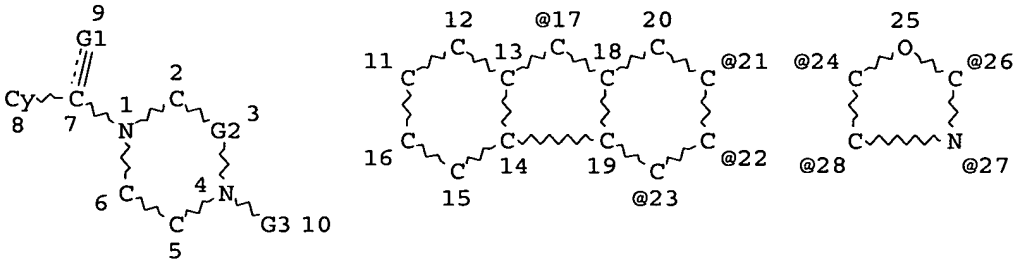

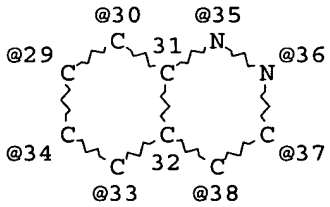

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DEFAULT MLEVEL IS ATOM
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STEREO ATTRIBUTES: NONE
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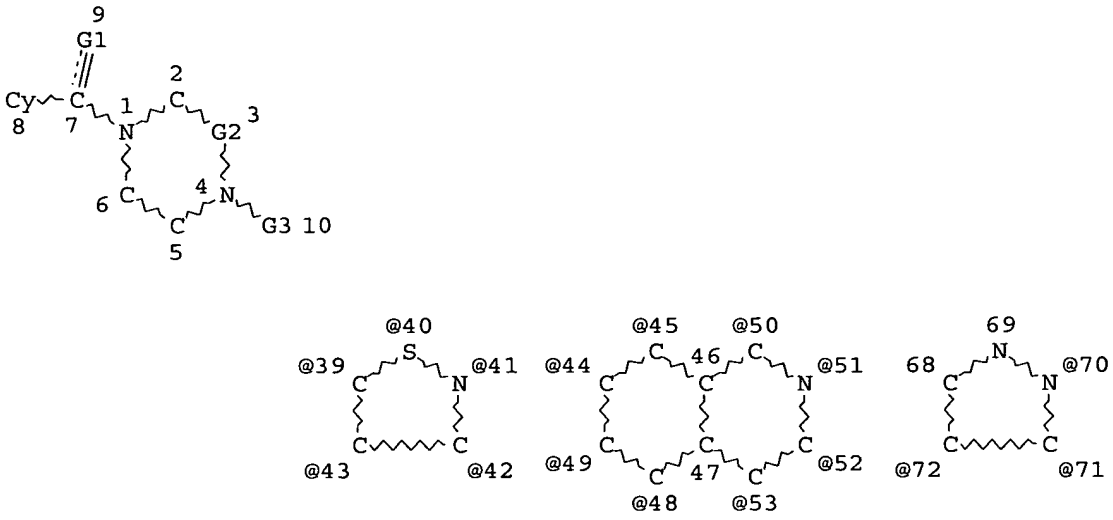

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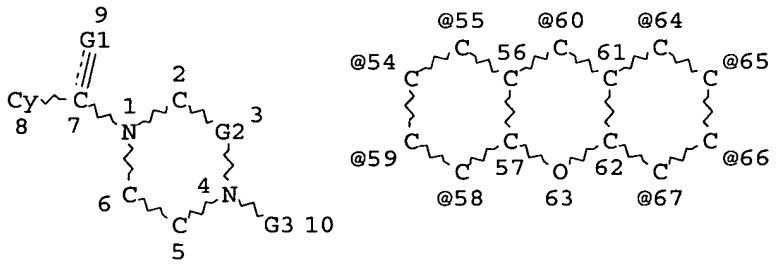

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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 24

STEREO ATTRIBUTES: NONE
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L20 31 SEA FILE=HCAPLUS ABB=ON PLU=ON L19

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=> d ibib abs hitstr l20 1-31

L20  ANSWER 1 OF 31  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:756697  HCAPLUS
DOCUMENT NUMBER:          141:260772
TITLE:                    Preparation of N-arylheteroaryls, in particular
                          N-phenylpiperazinyl methanones, as inhibitors of
                          tubulin polymerization and their compositions for
                          treatment of cancer
INVENTOR(S):              Le-Brun, Alain; Thompson, Fabienne; Tiraboschi,
                          Gilles; Mailliet, Patrick; Salvino, Joseph M.
PATENT ASSIGNEE(S):       Aventis Pharma S.A., Fr.
SOURCE:                   PCT Int. Appl., 197 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 French
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004078732         A1    20040916    WO 2004-FR168            20040126
     WO 2004078732         B1    20041028
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
             MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
             GQ, GW, ML, MR, NE, SN, TD, TG
     FR 2850379            A1    20040730    FR 2003-894              20030128
PRIORITY APPLN. INFO.:                       FR 2003-894          A   20030128
                                             FR 2003-13086        A   20031107

OTHER SOURCE(S):          MARPAT 141:260772
GI
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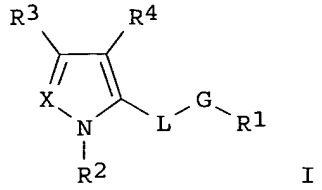

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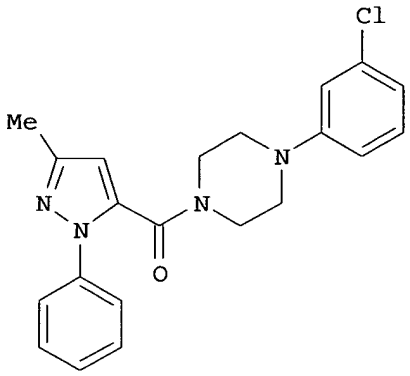


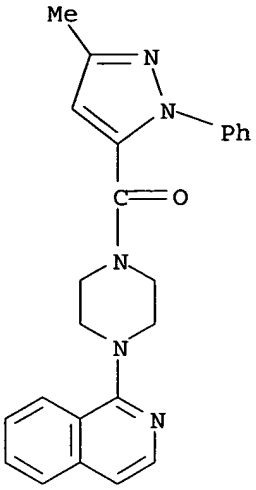
II

AB Title compds. I [wherein R1, R2 = independently (un)substituted hetero/aryl; L = CH2 and derivs., C(:O), C(:S), C:NOH and derivs.; R2 = (C5-C7)cycloalkyl; R3 = independently H, OH and derivs., S(O)nH and derivs., NH2 and derivs., halo, cycloalkylene, (un)substituted hetero/aryl, cycloalkyl, alkyl, etc.; R4 = H, alk(en/yn)yl, cyclopropyl, alkoxy, S-alkyl, F, Cl, Br; n = 0-2; X = N, CH; G = substituted piperazine, piperidine, 1,2,5,6-tetrahydropyridine; their racemics, stereoisomers, tautomers, prodrugs, and pharmaceutically acceptable salts] were prepared as inhibitors of tubulin polymerization and of tumor and endothelial cell proliferation in vitro, and for use in treatment of cancer. A combinatorial library of N-phenylpiperazinyl pyrazolyl ketones is given. For example, II was prepared from 5-methyl-2-phenyl-2H-pyrazole-3-carboxylic acid and 1-(3-chlorophenyl)piperazine. II gave an IC50 of 0.2 μM for inhibition of tubulin polymerization, an IC50 value of 0.002 μM for inhibition of HCT116 cells proliferation, and a 22% detachment of the endothelial HDMEC cells at a concentration of 1 μM. Thus, I and their pharmaceutical compns. are useful for treating cancer (no data).

IT **756751-64-1P**, [4-(Isoquinolin-1-yl)piperazin-1-yl](5-methyl-2-phenyl-2H-pyrazol-3-yl)methanone hydrochloride **756752-02-0P**, [4-(Isoquinolin-4-yl)piperazin-1-yl](5-methyl-2-phenyl-2H-pyrazol-3-yl)methanone
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor of tubulin polymerization; preparation of N-arylheteroaryls, in particular N-phenylpiperazinyl methanones, as inhibitors of tubulin polymerization and their compns. for treatment of cancer)

RN 756751-64-1 HCAPLUS

CN Piperazine, 1-(1-isoquinolinyl)-4-[(3-methyl-1-phenyl-1H-pyrazol-5-yl)carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 756752-02-0 HCAPLUS
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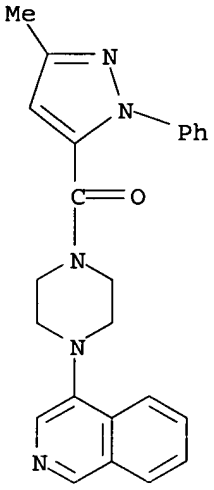

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:546484 HCAPLUS
DOCUMENT NUMBER: 141:106462
TITLE: Preparation of pyrazoles as inhibitors of HSP90
INVENTOR(S): Beswick, Mandy Christine; Drysdale, Martin James; Dymock, Brian William; McDonald, Edward
PATENT ASSIGNEE(S): Vernalis Cambridge Limited, UK; Cancer Research

Technology Ltd.; The Institute of Cancer Research
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056782	A1	20040708	WO 2003-GB5501	20031218

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-29618 A 20021219
OTHER SOURCE(S): MARPAT 141:106462
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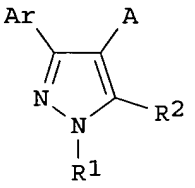

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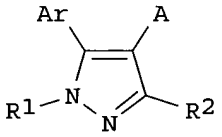


II

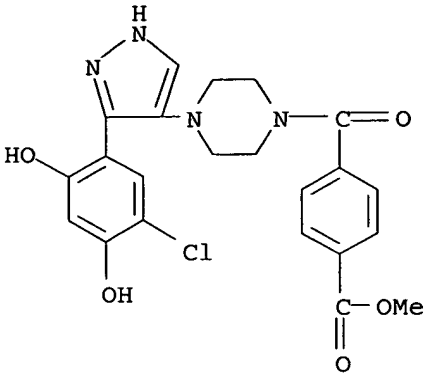
AB The title compds. [I or II; Ar = (un)substituted aryl, arylalkyl, heteroaryl, heteroarylalkyl; R1 = H, alkyl; R2 = H, (un)substituted cycloalkyl, cycloalkenyl, alkyl, alkenyl, alkynyl, carboxyl, carboxamide or carboxyl ester group; A = non-aromatic carbocyclic or heterocyclic ring wherein (i) a ring carbon is optionally substituted, and/or (ii) a ring nitrogen is optionally substituted by a group of formula -(Alk1)p(Cyc)n(Alk3)m(Z)r(Alk2)sQ where Alk1, Alk2 and Alk3 = alkyl; Cyc = carbocyclic or heterocyclic radical; m, n, p, r and s = 0-1; Z = O, S, CO, SO2, etc.; Q = H, (un)substituted carbocyclic or heterocyclic radical] which are inhibitors of HSP90, and are of value in the treatment of diseases responsive to HSP90 inhibition such as cancer, were prepared E.g., a multi-step synthesis of 4-chloro-6-(4-piperazin-1-yl-1H-pyrazol-3-yl)benzene-1,3-diol which showed IC50 of <50 μM in the malachite green ATPase assay, was given.

IT **719287-58-8P 719287-61-3P 719287-62-4P**
719287-63-5P 719287-64-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazoles as inhibitors of HSP90)

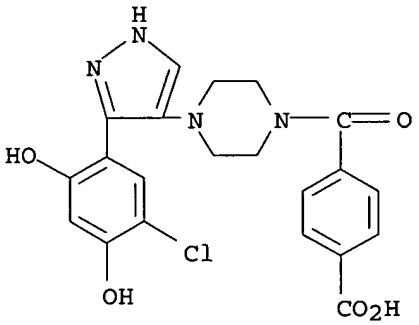
RN 719287-58-8 HCAPLUS

CN Benzoic acid, 4-[[4-[3-(5-chloro-2,4-dihydroxyphenyl)-1H-pyrazol-4-yl]-1-

piperazinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 719287-61-3 HCAPLUS
CN Benzoic acid, 4-[[4-[3-(5-chloro-2,4-dihydroxyphenyl)-1H-pyrazol-4-yl]-1-piperazinyl]carbonyl]- (9CI) (CA INDEX NAME)



RN 719287-62-4 HCAPLUS
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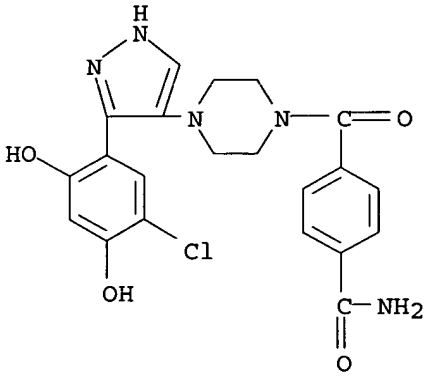
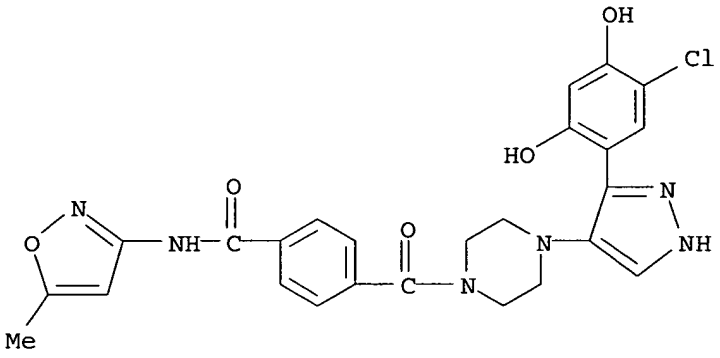
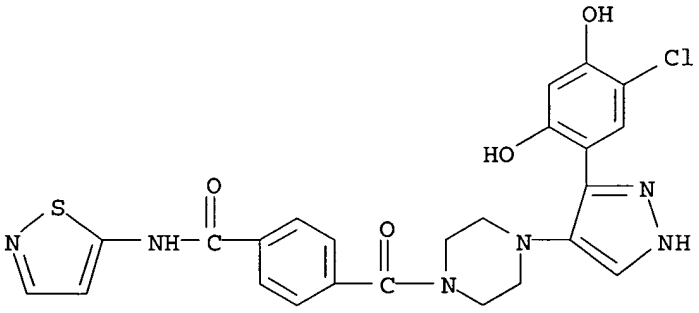


RN 719287-63-5 HCAPLUS

CN Benzamide, 4-[[4-[3-(5-chloro-2,4-dihydroxyphenyl)-1H-pyrazol-4-yl]-1-piperazinyl]carbonyl]-N-(5-methyl-3-isoxazolyl)- (9CI) (CA INDEX NAME)



RN 719287-64-6 HCAPLUS
CN Benzamide, 4-[[4-[3-(5-chloro-2,4-dihydroxyphenyl)-1H-pyrazol-4-yl]-1-piperazinyl]carbonyl]-N-5-isothiazolyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:182866 HCAPLUS
DOCUMENT NUMBER: 140:236096
TITLE: Preparation of proline derivatives as antibacterial agents
INVENTOR(S): Fujita, Masahiro; Sakamoto, Masato; Horiuchi, Nobuhiko; Yamamoto, Takayoshi; Tomita, Kyoji; Mizuno, Kazuhiro; Niga, Toshiyuki; Ito, Hideaki; Kashimoto, Shigeki
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018453	A1	20040304	WO 2003-JP10548	20030821

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PRIORITY APPLN. INFO.: JP 2002-242795 A 20020823
JP 2002-339200 A 20021122
JP 2003-27010 A 20030204
OTHER SOURCE(S): MARPAT 140:236096
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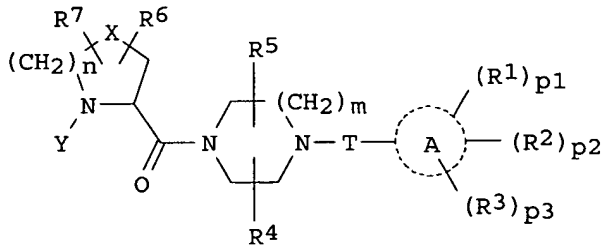

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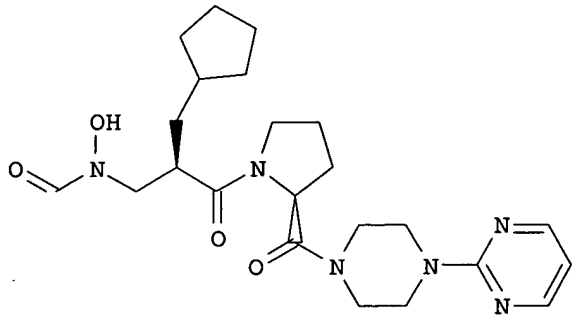


II

AB Proline derivs. represented by the general formula (I) or salts thereof [wherein A = a group derived from a 5- or 6-membered heterocycle which may be fused with an optionally halogenated benzene ring; p1, p2, p3 = 0, 1; R1, R2, R3 = H, lower alkoxy, lower alkylthio, halo,HO, (un)protected or (un)substituted NH2 or CONH2, hydroxy-lower alkylamino, CO2H, lower alkoxycarbonyl, lower alkylcarbonyloxy, (un)substituted lower alkylsulfonyloxy, cyano; when p1 = p2 = 1, CR1R2 = CO; or when p1 = p2 = p3 = 1, R1 = R2 = H and R3 = a 5- or 6-membered saturated or unsatd. cyclic group; T = a single bond, CH2, CO; R4, R5 = H, lower alkyl; or CR4R5 = CO; n, m = 1,2; R6, R7 = H, OH, halogeno, lower alkyl, Ph, lower alkoxy, phenyl-lower alkyl, (un)protected NH2; R6 and R7 together form a saturated cyclic group; X = CH2, CH, S, O; Y = H, an amino-protecting group, or a group represented by the general formula R9ON(CHO)CH2CH(R8)CO; wherein R8 = alkyl, cycloalkyl-lower alkyl; R9 = H, a hydroxyl-protecting group, etc.] are prepared These compds. are useful as antibacterial drugs against multidrug-resistant bacteria. Thus, (2R)-3-cyclopentyl-2-[[N-(2,4-

dimethoxybenzyloxy)-N-formylamino]methyl]propionic acid was condensed with (2S)-2-[[4-(2-pyrimidinyl)-1-piperazinyl]carbonyl]pyrrolidine hydrochloride using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, 1-hydroxybenzotriazole, and Et3N in CH2Cl2 at room temperature for 18 h to give 68% (2S)-1-[(2R)-3-cyclopentyl-2-[[N-(2,4-dimethoxybenzyloxy)-N-formylamino]methyl]propionyl]-2-[[4-(2-pyrimidinyl)-1-piperazinyl]carbonyl]pyrrolidine which was treated with 3% CF3CO2H in CH2Cl2 at room temperature for 17 h and then with saturated aqueous NaHCO3 under ice-cooling to give 77% (2S)-1-[(2R)-3-cyclopentyl-2-[(N-formyl-N-hydroxyamino)methyl]propionyl]-2-[[4-(2-pyrimidinyl)-1-piperazinyl]carbonyl]pyrrolidine (II). II showed min. inhibitory concentration of 0.25, 0.125, 0.03, 0.25, 0.5, 0.125, 1, 0.5, and 0.125 μg/mL against Staphylococcus aureus Smith, S. aureus KTO150 (MRSA), S. epidermidis ATCC12228, Streptococcus pneumoniae ATCC49619, S. pneumoniae KT2524 (PRSP), S. pneumoniae KB2534 (PRSP), S. pyrogenes ATCC12344, Enterococcus faecium ATCC19434, and Moraxella (B.) catarrhalis K1209, resp.

IT **668483-08-7P 668483-38-3P**

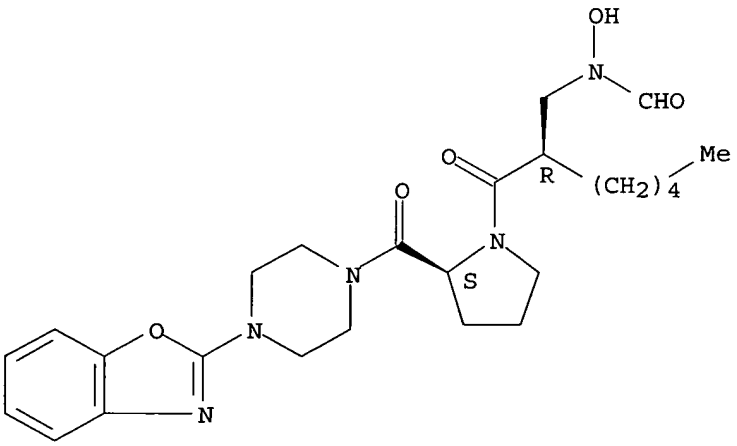
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of proline derivs. as antibacterial agents against multidrug-resistant bacteria)

RN 668483-08-7 HCAPLUS

CN Piperazine, 1-(2-benzoxazolyl)-4-[(2R)-N-formyl-N-hydroxy-2-pentyl-β-alanyl-L-prolyl]- (9CI) (CA INDEX NAME)

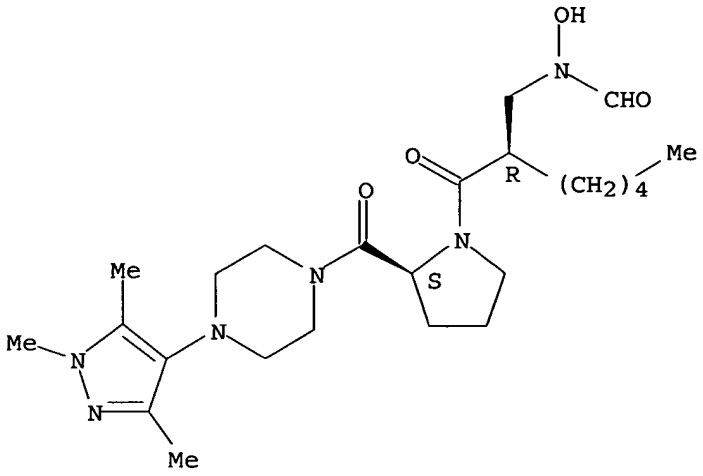
Absolute stereochemistry.



RN 668483-38-3 HCAPLUS

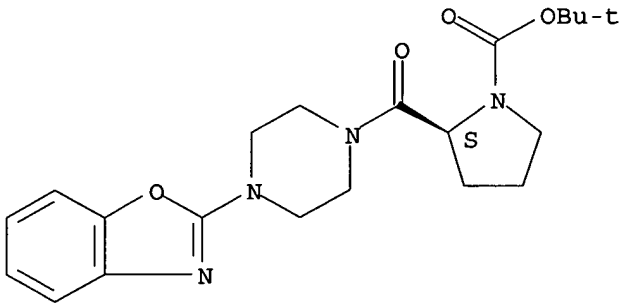
CN Piperazine, 1-[(2R)-N-formyl-N-hydroxy-2-pentyl-β-alanyl-L-prolyl]-4-(1,3,5-trimethyl-1H-pyrazol-4-yl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



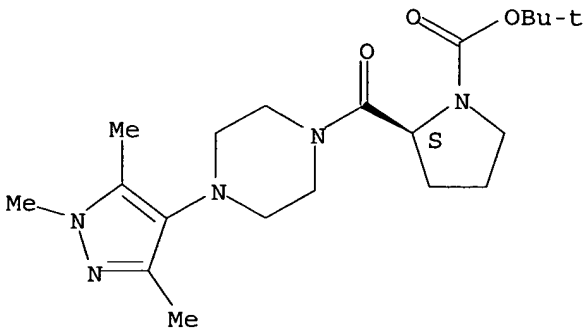
IT **668485-02-7P 668485-04-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of proline derivs. as antibacterial agents against multidrug-resistant bacteria)
RN 668485-02-7 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[4-(2-benzoxazolyl)-1-piperazinyl]carbonyl]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 668485-04-9 HCAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-[[4-(1,3,5-trimethyl-1H-pyrazol-4-yl)-1-piperazinyl]carbonyl]-, 1,1-dimethylethyl ester, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 4 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:421123 HCAPLUS
DOCUMENT NUMBER: 139:190693
TITLE: Targeting Tuberculosis and Malaria through Inhibition of Enoyl Reductase: Compound Activity and Structural Data
AUTHOR(S): Kuo, Mack R.; Morbidoni, Hector R.; Alland, David; Sneddon, Scott F.; Gourlie, Brian B.; Staveski, Mark M.; Leonard, Marina; Gregory, Jill S.; Janjigian, Andrew D.; Yee, Christopher; Musser, James M.; Kreiswirth, Barry; Iwamoto, Hiroyuki; Perozzo, Remo; Jacobs, William R., Jr.; Sacchettini, James C.; Fidock, David A.
CORPORATE SOURCE: Department of Biochemistry and Biophysics, Texas A & M University, College Station, TX, 77843, USA
SOURCE: Journal of Biological Chemistry (2003), 278(23), 20851-20859
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

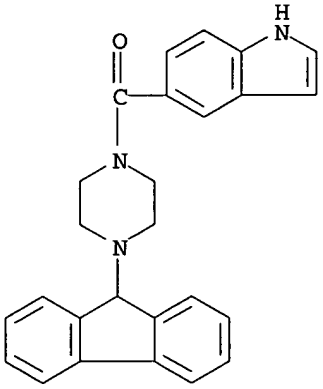
AB Tuberculosis and malaria together result in an estimated 5 million deaths annually. The spread of multidrug resistance in the most pathogenic causative agents, Mycobacterium tuberculosis and Plasmodium falciparum, underscores the need to identify active compds. with novel inhibitory properties. Although genetically unrelated, both organisms use a type II fatty-acid synthase system. Enoyl acyl carrier protein reductase (ENR), a key type II enzyme, has been repeatedly validated as an effective antimicrobial target. Using high throughput inhibitor screens with a combinatorial library, the authors have identified two novel classes of compds. with activity against the M. tuberculosis and P. falciparum enzyme (referred to as InhA and PfENR, resp.). The crystal structure of InhA complexed with NAD+ and one of the inhibitors was determined to elucidate the mode of binding. Structural anal. of InhA with the broad spectrum antimicrobial triclosan revealed a unique stoichiometry where the enzyme contained either a single triclosan mol., in a configuration typical of other bacterial ENR:triclosan structures, or harbored two triclosan mols. bound to the active site. Significantly, these compds. do not require activation and are effective against wild-type and drug-resistant strains of M. tuberculosis and P. falciparum. Moreover, they provide broader chemical diversity and elucidate key elements of inhibitor binding to InhA

for subsequent chemical optimization.

IT **353522-10-8**, Genz 10850
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting tuberculosis and malaria through inhibition of enoyl reductase in relation to compound activity and structural data and overcoming resistance and NAD+ binding)

RN 353522-10-8 HCAPLUS

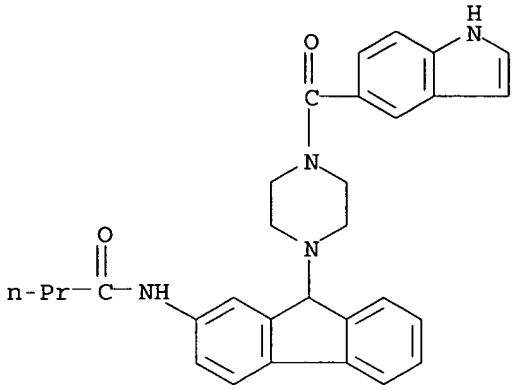
CN Piperazine, 1-(9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



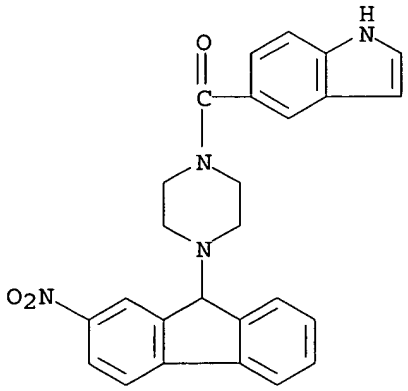
IT **353522-64-2**, Genz 13108 **353522-74-4**, Genz 12644
353522-76-6, Genz 12645 **353522-77-7**, Genz 12646
586368-25-4, Genz 11918 **586368-28-7**, Genz 12637
586368-29-8, Genz 12638 **586368-31-2**, Genz 12639
586368-33-4, Genz 12640 **586368-34-5**, Genz 12641
586368-35-6, Genz 12643 **586368-40-3**, Genz 13100
586368-43-6, Genz 13347 **586368-45-8**, Genz 13348
586368-47-0, Genz 13349
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting tuberculosis and malaria through inhibition of enoyl reductase in relation to compound activity and structural data and overcoming resistance and NAD+ binding)

RN 353522-64-2 HCAPLUS

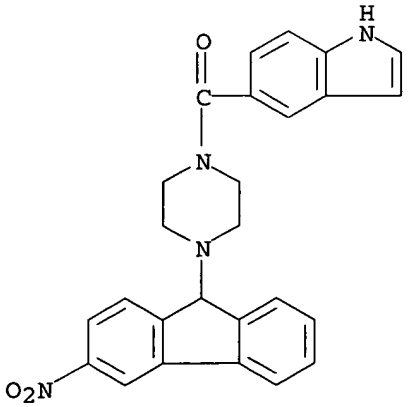
CN Butanamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



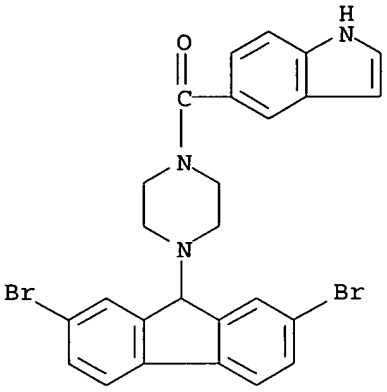
RN 353522-74-4 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(2-nitro-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



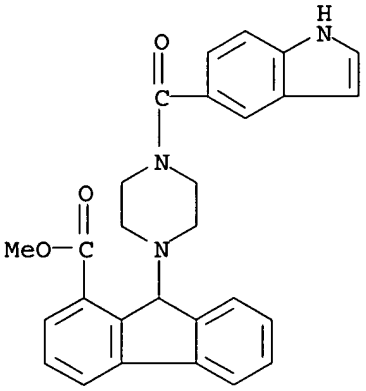
RN 353522-76-6 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(3-nitro-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



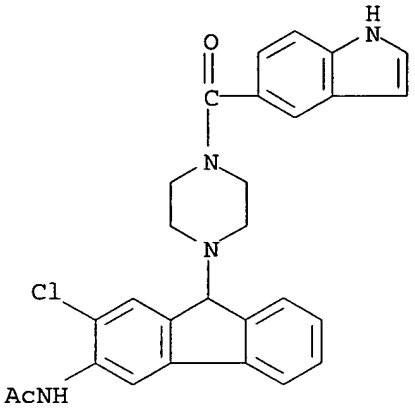
RN 353522-77-7 HCAPLUS
CN Piperazine, 1-(2,7-dibromo-9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)-
(9CI) (CA INDEX NAME)



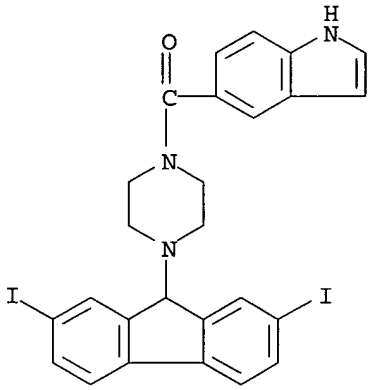
RN 586368-25-4 HCAPLUS
CN 9H-Fluorene-1-carboxylic acid, 9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-
, methyl ester (9CI) (CA INDEX NAME)



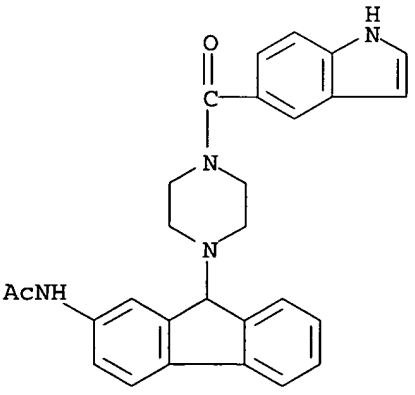
RN 586368-28-7 HCAPLUS
CN Acetamide, N-[2-chloro-9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-
fluoren-3-yl]- (9CI) (CA INDEX NAME)



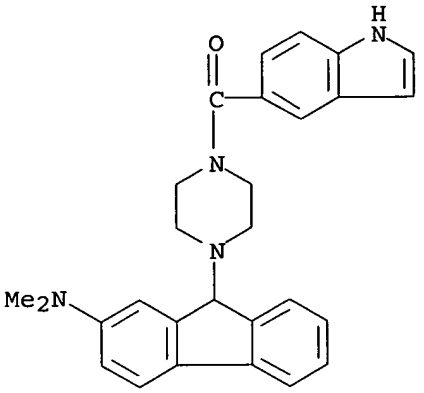
RN 586368-29-8 HCAPLUS
CN Piperazine, 1-(2,7-diiodo-9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)-
(9CI) (CA INDEX NAME)



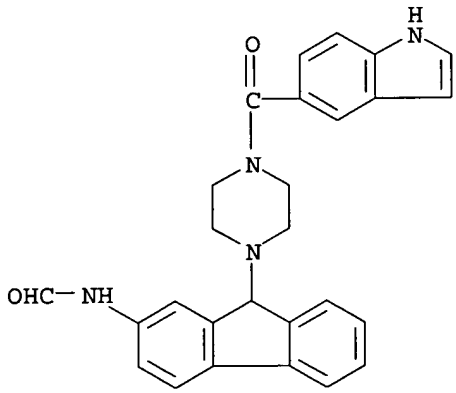
RN 586368-31-2 HCAPLUS
CN Acetamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]-
(9CI) (CA INDEX NAME)



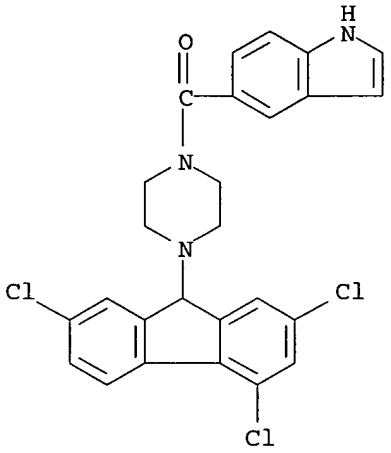
RN 586368-33-4 HCAPLUS
CN Piperazine, 1-[2-(dimethylamino)-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



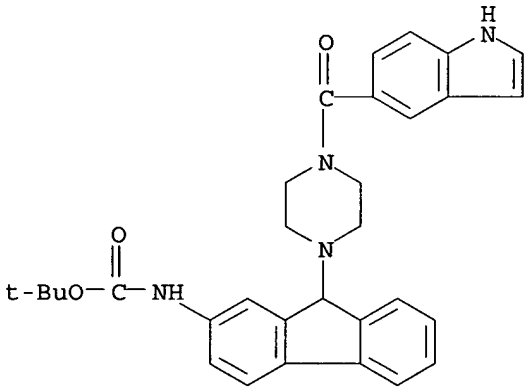
RN 586368-34-5 HCAPLUS
CN Piperazine, 1-[2-(formylamino)-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



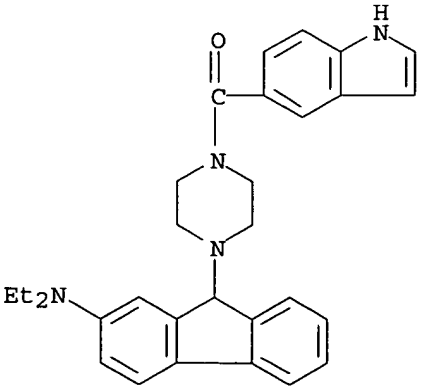
RN 586368-35-6 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(2,4,7-trichloro-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



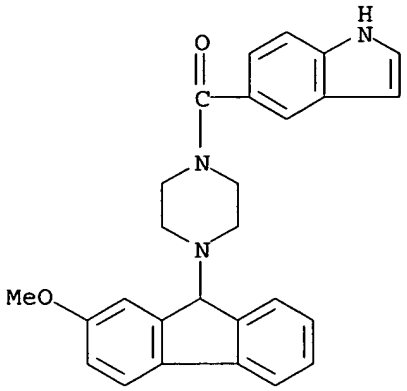
RN 586368-40-3 HCAPLUS
CN Carbamic acid, [9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



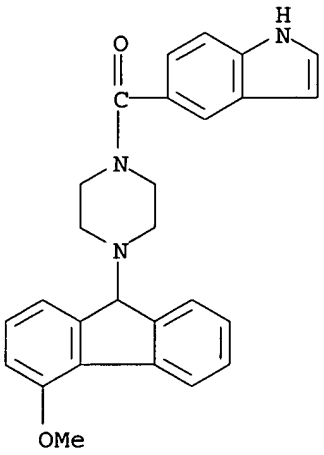
RN 586368-43-6 HCAPLUS
CN Piperazine, 1-[2-(diethylamino)-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



RN 586368-45-8 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(2-methoxy-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



RN 586368-47-0 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(4-methoxy-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



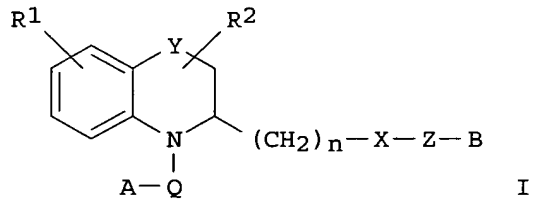
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 5 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:301077 HCAPLUS
DOCUMENT NUMBER: 138:304309
TITLE: Preparation of 2-(heterocyclylalkyl)-1,2,3,4-tetrahydroquinolines and analogs as 5-HT1A receptor inhibitors for treatment of urinary tract disorders
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Riva, Carlo; Testa, Rodolfo; Corbett, Jeff W.
PATENT ASSIGNEE(S): Recordati S.A., Switz.; Recordati Industria Chimica e Farmaceutica S.p.A.
SOURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2

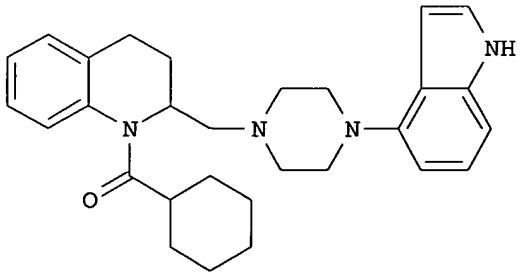
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031436	A1	20030417	WO 2002-EP11282	20021007
WO 2003031436	C1	20040527		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2458456	AA	20030417	CA 2002-2458456	20021007
US 2003162777	A1	20030828	US 2002-266104	20021007
US 2003181446	A1	20030925	US 2002-266088	20021007
EP 1432701	A1	20040630	EP 2002-782863	20021007
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002013067	A	20040928	BR 2002-13067	20021007
JP 2005508952	T2	20050407	JP 2003-534419	20021007
ZA 2004003356	A	20041108	ZA 2004-3356	20040504
PRIORITY APPLN. INFO.:			IT 2001-MI2060 A	20011005
			US 2002-350680P P	20020122
			WO 2002-EP11282 W	20021007

OTHER SOURCE(S): MARPAT 138:304309
GI



I



II

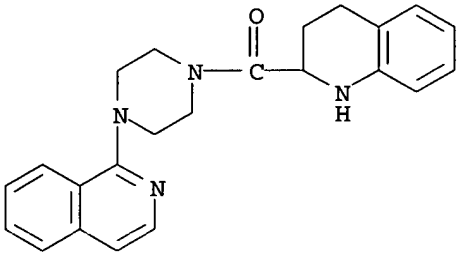
AB Title compds. I [wherein R1 = H, halo, OH, (halo)alkyl, (halo)alkoxy, NO2, NR3R4, or (un)substituted Ph or heterocyclyl; R2 = 1 or 2 substituents selected from H or alkyl; R3 and R4 = independently H, alkyl, acyl, or

alkoxycarbonyl; Y = a bond or CH2; Q = CO, CS, or SO2; A = (un)substituted (cyclo)alkyl, (cyclo)alkenyl, aryl, heterocyclyl, (di)alkylamino, arylamino, or arylalkylamino; n = 1 or 2; X = (un)substituted piperidinyl or piperazinyl; Z = a bond, O, S, CH2, CH2CH2, CO, CHOH, OCH2, NH, NHCO, or NHCONHCH2; or ZB = 2,3-dihydrobenzo[1,4]dioxin-2-yl; B = (un)substituted monocyclic or bicyclic (hetero)aryl; with provisos; and enantiomers, diastereomers, N-oxides, crystalline forms, hydrates, solvates, or pharmaceutically acceptable salts thereof] were prepared as serotonergic receptor antagonists. For example, coupling of 2-chloromethylquinoline with 1-(4-indolyl)piperazine in the presence of DIPEA in DMF gave 1-(4-indolyl)-4-(quinolin-2-ylmethyl)piperazine (70%), which was hydrogenated using PtO2/AcOH/H2 to provide the tetrahydroquinoline derivative (76.5%). Amidation with cyclohexanecarbonyl chloride in the presence of TEA in CH2Cl2 afforded II (81%). The (+)- and (-)-enantiomers were separated via chiral column chromatog. II inhibited the human 5HT1A-serotonergic receptor in transfected HeLa cells with Ki of 3.3 nM, while (+)-II showed a binding affinity with Ki of 0.2 nM. Similarly, (+)-II proved more effective than II in suppressing the frequency of rhythmic bladder-voiding contractions in rats with ED50 values of 24 μg/kg and 64 μg/kg, resp. In addition, (+)-II exhibited significant and long-lasting post-synaptic 5-HT1A-receptor antagonist activity by suppressing forepaw treading induced by 8-OH-DPAT in rats with 100% inhibition after 0.5 h and 98% inhibition after 4 h of administration of a dose of 1 mg/kg p.o. By contrast, (-)-II showed only 19% inhibition after 0.5 h and 5% inhibition after 4 h of administration of a dose of 1 mg/kg p.o.

IT **511230-37-8P**, 1-(1-Isoquinolinyl)-4-(1,2,3,4-tetrahydroquinolin-2-ylcarbonyl)piperazine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of (aminoalkyl)- and (heterocyclylalkyl)tetrahydroquinoline 5-HT1A antagonists from haloalkylquinolines and amines or heterocycles for treatment of urinary tract and CNS disorders)

RN 511230-37-8 HCAPLUS

CN Piperazine, 1-(1-isoquinolinyl)-4-[(1,2,3,4-tetrahydro-2-quinolinyl)carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 6 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:574925 HCAPLUS

DOCUMENT NUMBER: 137:140442

TITLE: Preparation of 1,5-diaryl-7-heterocyclyl(alkyl)-2-quinolinones as p38 protein kinase inhibitors

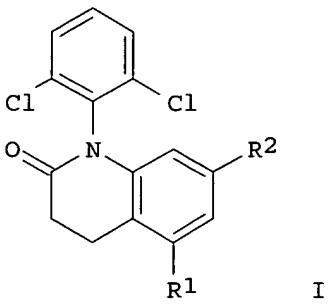
INVENTOR(S): Doherty, James B.; Stelmach, John E.; Chen, Meng-Hsin; Liu, Luping; Hunt, Julianne A.; Ruzek, Rowena D.; Goulet, Joung L.; Wisnoski, David D.; Natarajan,

Swaminathan Ravi; Rupprecht, Kathleen M.; Bao, Jianming; Miao, Shouwu; Hong, Xingfang
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 440 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002058695	A1	20020801	WO 2001-US48676	20011214
WO 2002058695	C2	20030912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2431904	AA	20020801	CA 2001-2431904	20011214
EP 1345603	A1	20030924	EP 2001-994260	20011214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521892	T2	20040722	JP 2002-559029	20011214
US 2003092712	A1	20030515	US 2001-23231	20011217
US 6809199	B2	20041026		

PRIORITY APPLN. INFO.: US 2000-256822P P 20001220
WO 2001-US48676 W 20011214

OTHER SOURCE(S): MARPAT 137:140442
GI



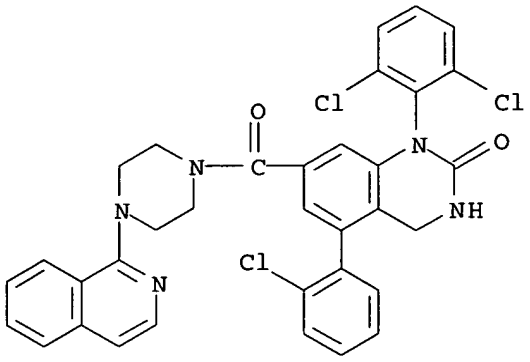
I

AB Title compds. were prepared Thus, 2,6-dibromo-4-methoxytoluene was converted in 5 steps to arylquinolinone I (R1 = Br, R2 = OMe) which was condensed with 2,4-F2C6H3B(OH)2 and the O-demethylated product converted in 4 steps to I (R1 = C6H3F2-2,4, R2 = 4-piperidinyl). Data for biol. activity of title compds. were given.

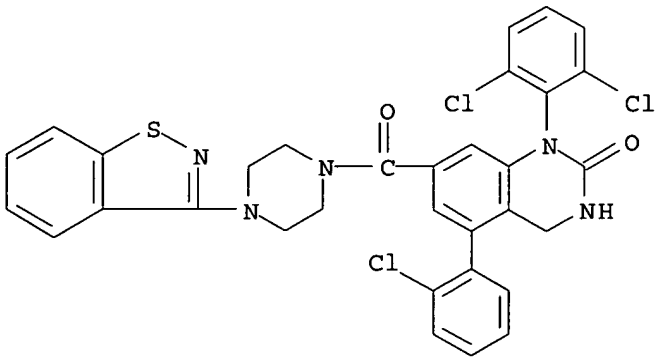
IT **444660-29-1P 444660-31-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of 1,5-diaryl-7-heterocyclyl(alkyl)-2-quinolinones as p38 protein kinase inhibitors)

RN 444660-29-1 HCAPLUS
CN Piperazine, 1-[[5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-1,2,3,4-tetrahydro-2-oxo-7-quinazolinyl]carbonyl]-4-(1-isoquinolinyl)- (9CI) (CA INDEX NAME)



RN 444660-31-5 HCAPLUS
CN Piperazine, 1-(1,2-benzisothiazol-3-yl)-4-[[5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-1,2,3,4-tetrahydro-2-oxo-7-quinazolinyl]carbonyl]- (9CI) (CA INDEX NAME)



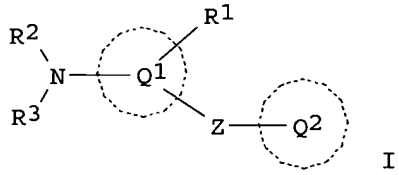
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 7 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:487561 HCAPLUS
DOCUMENT NUMBER: 137:63240
TITLE: Preparation of thiazolyl inhibitors of Tec family tyrosine kinases
INVENTOR(S): Barrish, Joel C.; Das, Jagabandhu; Kanner, Steven B.; Liu, Chunjian; Spergel, Steven H.; Witayk, John; Doweyko, Arthur M. P.; Furch, Joseph A.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002050071	A1	20020627	WO 2001-US49430	20011219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2433018	AA	20020627	CA 2001-2433018	20011219
AU 2002031139	A5	20020701	AU 2002-31139	20011219
EP 1347971	A1	20031001	EP 2001-991416	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2005506950	T2	20050310	JP 2002-551567	20011219
US 2003069238	A1	20030410	US 2001-27982	20011220
US 6706717	B2	20040316		
US 2004067989	A1	20040408	US 2003-641876	20030815
US 2004067990	A1	20040408	US 2003-641933	20030815
US 2004077695	A1	20040422	US 2003-641535	20030815
US 2004110752	A1	20040610	US 2003-642040	20030815
PRIORITY APPLN. INFO.:			US 2000-257830P	P 20001221
			WO 2001-US49430	W 20011219
			US 2001-27982	A3 20011220

OTHER SOURCE(S): MARPAT 137:63240
GI



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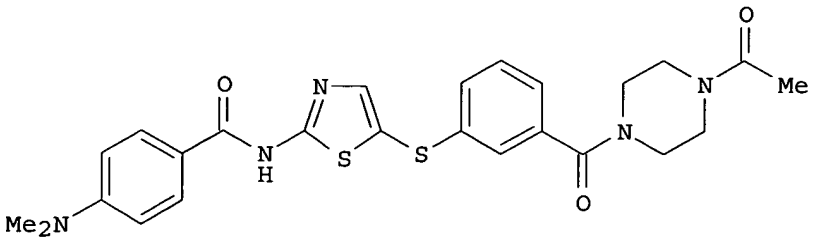


II

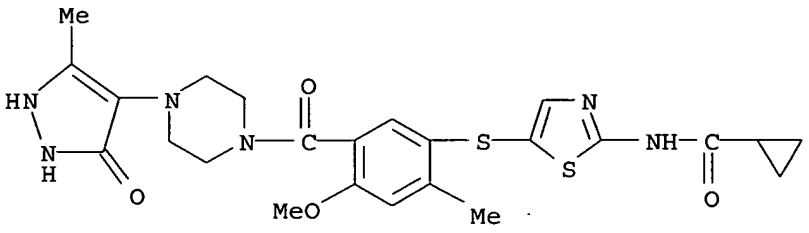
AB The title compds. [I; Q1 = thiazolyl; Q2 = (un)substituted (hetero)aryl; Z = O, S, NR4, etc.; R1 = H, OH, SH, etc.; R2, R3 = H, (un)substituted (hetero)aryl, (hetero)arylcarbonyl, etc.; R4 = H, alkyl, aryl, etc.], useful in the treatment of Tec family tyrosine kinase-associated disorders such as cancer, immunol. disorders and allergic disorders, were prepared

E.g., a multi-step synthesis of the thiazole II, was given.

IT **439576-57-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of thiazolyl inhibitors of Tec family tyrosine kinases)

RN 439576-57-5 HCAPLUS

CN Cyclopropanecarboxamide, N-[5-[[5-[[4-(2,3-dihydro-5-methyl-3-oxo-1H-pyrazol-4-yl)-1-piperazinyl]carbonyl]-4-methoxy-2-methylphenyl]thio]-2-thiazolyl]- (9CI) (CA INDEX NAME)

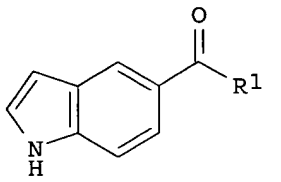


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

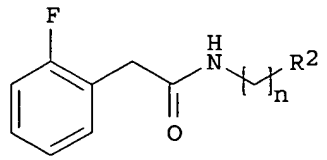
L20 ANSWER 8 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:581832 HCAPLUS
DOCUMENT NUMBER: 135:166842
TITLE: Preparation of (1H-indol-5-yl)methanones, 2-(2-fluorophenyl)acetamides and 2-(pyrazol-1-yl)pyrimidines as InhA inhibitors
INVENTOR(S): Staveski, Mark M.; Sneddon, Scott F.; Yee, Christopher; Janjigian, Andrew
PATENT ASSIGNEE(S): Genzyme Corporation, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001056974	A2	20010809	WO 2001-US40045	20010206
WO 2001056974	A3	20020718		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6372752	B1	20020416	US 2000-499183	20000207
PRIORITY APPLN. INFO.:			US 2000-499183	A1 20000207

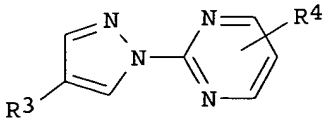
OTHER SOURCE(S): MARPAT 135:166842
GI



I



II



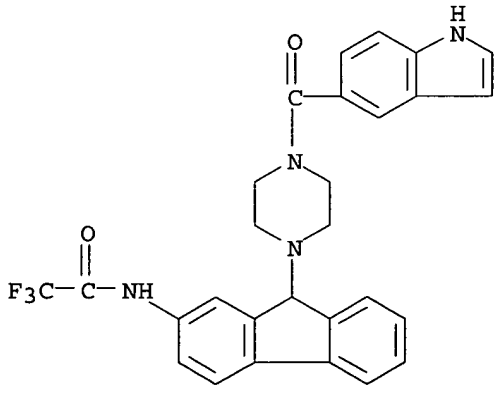
III

AB The title compds. [I-III, etc.; R1 = (un)substituted heteroaryl, piperazinyl, piperidinyl, etc.; R2 = OH, (un)substituted aryl, cycloalkyl, etc.; n = 1-2; R3 = (un)substituted Ph, heteroaryl; R4 = H, halo, alkyl, etc.] which inhibit the Mycobacterial enoyl-ACP reductase required for cell wall biosynthesis, and are useful for treating a bacterial infection in a patient, were prepared Thus, reacting 2-fluorophenylacetic acid with 4-chlorophenethylamine in the presence of DMAP and EDCI in CH2Cl2 afforded II [R2 = 4-ClC6H4; n = 2] which showed 82% InhA inhibition at 40 μM.

IT **353522-11-9P 353522-12-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of (1H-indol-5-yl)methanones, 2-(2-fluorophenyl)acetamides and 2-(pyrazol-1-yl)pyrimidines as InhA inhibitors)

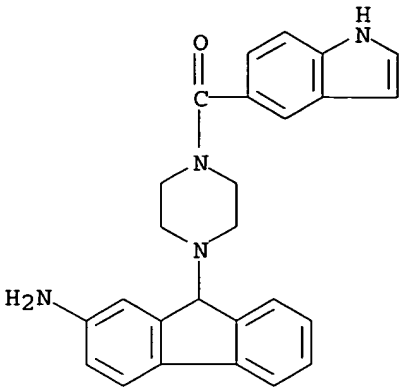
RN 353522-11-9 HCAPLUS

CN Acetamide, 2,2,2-trifluoro-N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



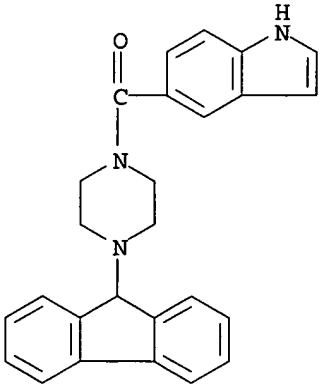
RN 353522-12-0 HCAPLUS

CN Piperazine, 1-(2-amino-9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)

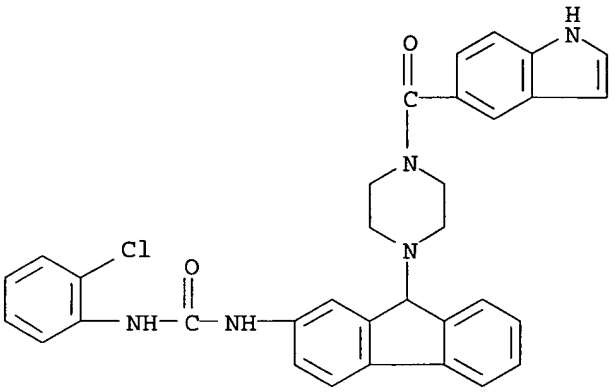


IT **353522-10-8P 353522-13-1P 353522-62-0P**
353522-63-1P 353522-64-2P 353522-65-3P
353522-66-4P 353522-67-5P 353522-68-6P
353522-69-7P 353522-71-1P 353522-73-3P
353522-74-4P 353522-76-6P 353522-77-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (1H-indol-5-yl)methanones, 2-(2-fluorophenyl)acetamides and 2-(pyrazol-1-yl)pyrimidines as InhA inhibitors)

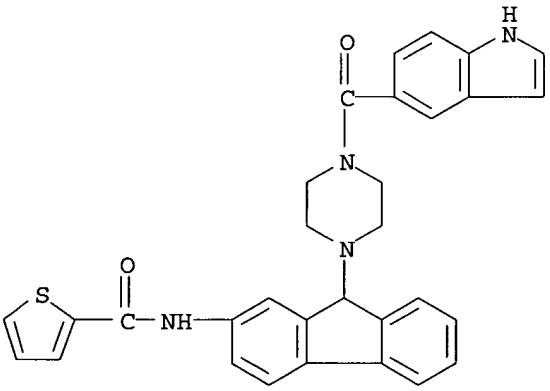
RN 353522-10-8 HCAPLUS
CN Piperazine, 1-(9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



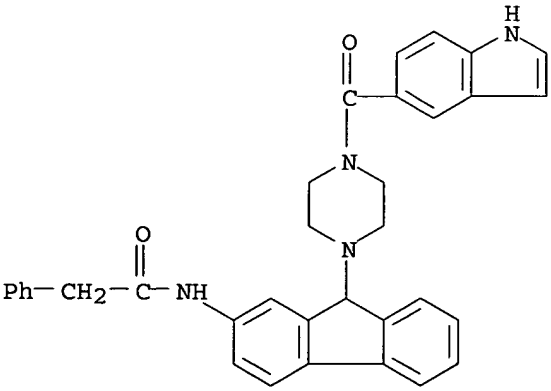
RN 353522-13-1 HCAPLUS
CN Piperazine, 1-[2-[[[(2-chlorophenyl)amino]carbonyl]amino]-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



RN 353522-62-0 HCAPLUS
CN 2-Thiophenecarboxamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)

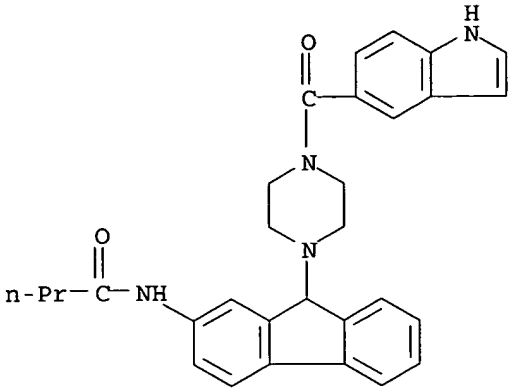


RN 353522-63-1 HCAPLUS
CN Benzeneacetamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)

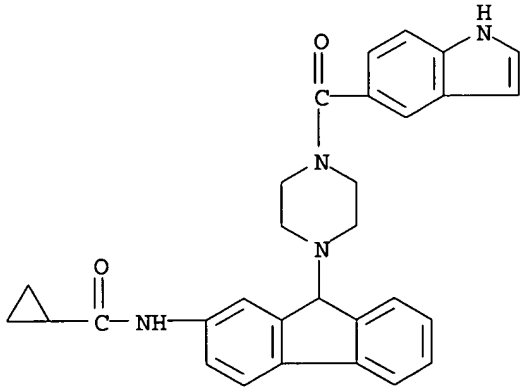


RN 353522-64-2 HCAPLUS

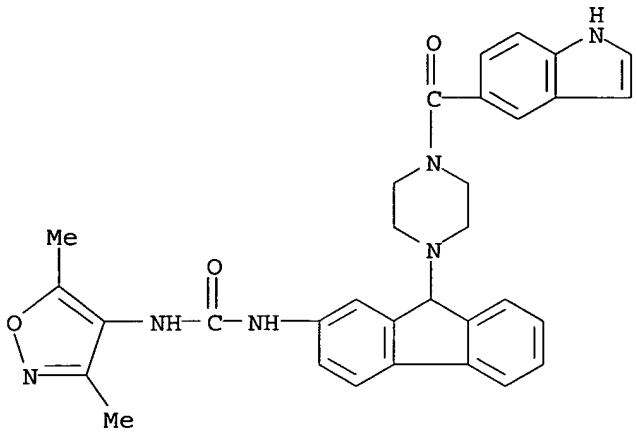
CN Butanamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



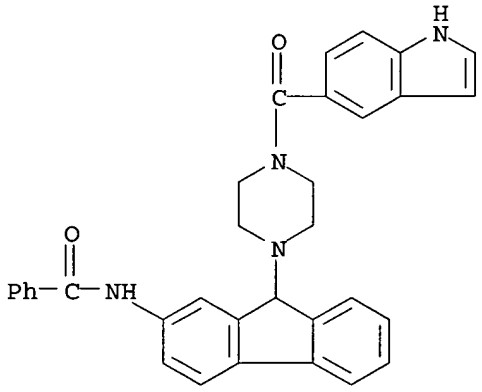
RN 353522-65-3 HCAPLUS
CN Cyclopropanecarboxamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



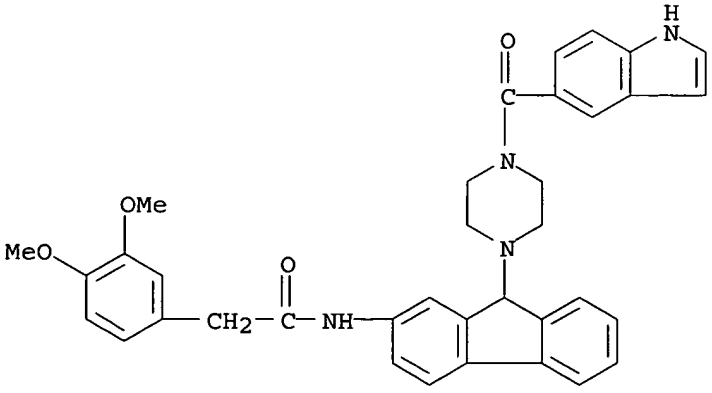
RN 353522-66-4 HCAPLUS
CN Piperazine, 1-[2-[[[(3,5-dimethyl-4-isoxazolyl)amino]carbonyl]amino]-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



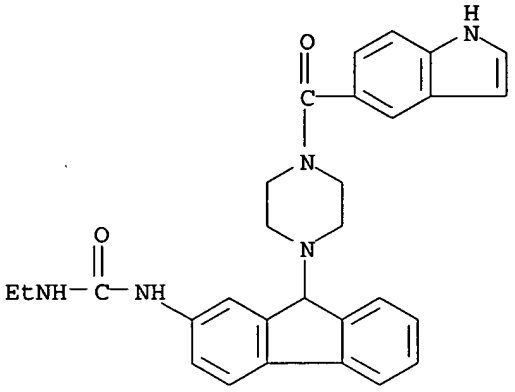
RN 353522-67-5 HCAPLUS
CN Benzamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



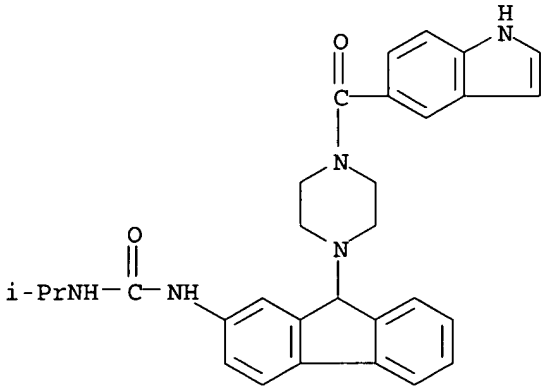
RN 353522-68-6 HCAPLUS
CN Benzeneacetamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]-3,4-dimethoxy- (9CI) (CA INDEX NAME)



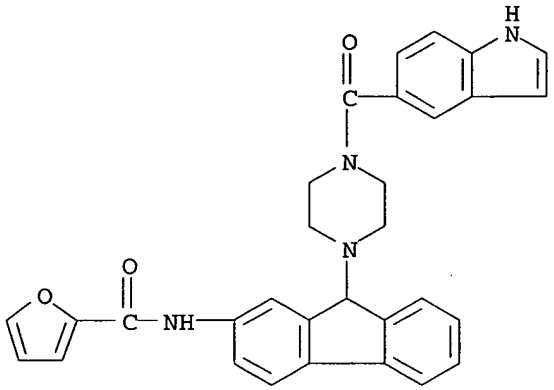
RN 353522-69-7 HCAPLUS
CN Piperazine, 1-[2-[[(ethylamino)carbonyl]amino]-9H-fluoren-9-yl]-4-(1H-indol-5-ylcarbonyl)- (9CI) (CA INDEX NAME)



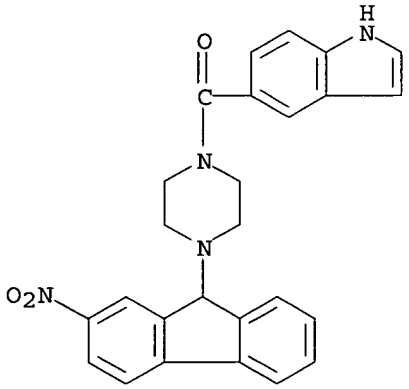
RN 353522-71-1 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-[2-[[[(1-methylethyl)amino]carbonyl]amino]-9H-fluoren-9-yl]- (9CI) (CA INDEX NAME)



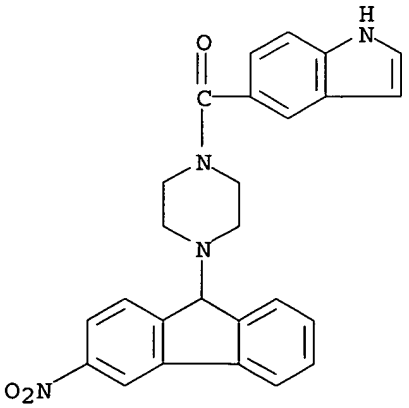
RN 353522-73-3 HCAPLUS
CN 2-Furancarboxamide, N-[9-[4-(1H-indol-5-ylcarbonyl)-1-piperazinyl]-9H-fluoren-2-yl]- (9CI) (CA INDEX NAME)



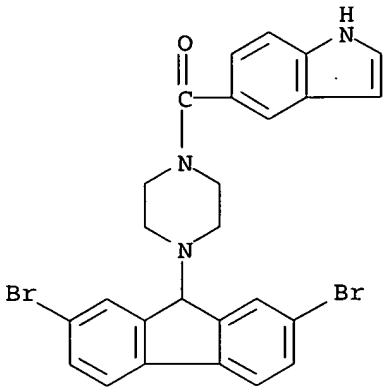
RN 353522-74-4 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(2-nitro-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



RN 353522-76-6 HCAPLUS
CN Piperazine, 1-(1H-indol-5-ylcarbonyl)-4-(3-nitro-9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)



RN 353522-77-7 HCAPLUS
CN Piperazine, 1-(2,7-dibromo-9H-fluoren-9-yl)-4-(1H-indol-5-ylcarbonyl)-(9CI) (CA INDEX NAME)



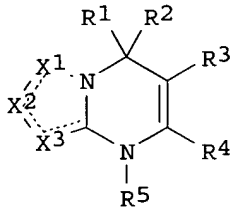
L20 ANSWER 9 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:416942 HCAPLUS
DOCUMENT NUMBER: 135:19660
TITLE: Preparation of pyrazolo[1,5-a]pyrimidines as potassium channel inhibitors
INVENTOR(S): Atwal, Karnail S.; Vaccaro, Wayne; Lloyd, John; Finlay, Heather; Yan, Lin; Bhandaru, Rao S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 298 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040231	A1	20010607	WO 2000-US32785	20001204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393809	AA	20010607	CA 2000-2393809	20001204
EP 1237891	A1	20020911	EP 2000-980930	20001204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000016166	A	20030624	BR 2000-16166	20001204
JP 2004507442	T2	20040311	JP 2001-540986	20001204
NZ 518663	A	20041126	NZ 2000-518663	20001204
AU 781862	B2	20050616	AU 2001-18127	20001204
US 2003022890	A1	20030130	US 2000-729731	20001205
US 6706720	B2	20040316		
ZA 2002003407	A	20030925	ZA 2002-3407	20020429

NO 2002002649	A	20020606	NO 2002-2649		20020605
US 2004063687	A1	20040401	US 2003-660878		20030912
PRIORITY APPLN. INFO.:			US 1999-169091P	P	19991206
			US 2000-236037P	P	20000928
			WO 2000-US32785	W	20001204
			US 2000-729731	A3	20001205

OTHER SOURCE(S): MARPAT 135:19660

GI



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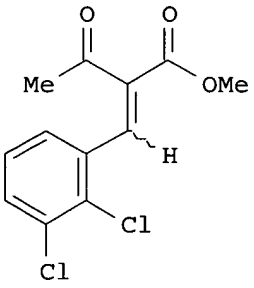
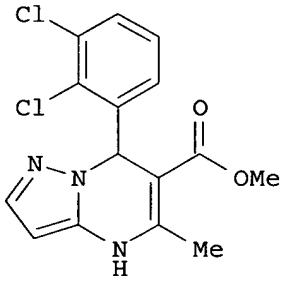


II



III

AB The title compds. [I; X1-X3 = N, NR6, (CR7)q, (CHR7)q, CO; R1-R7 = (CH2)n(Z1)m(CH2)pZ2; or R1-R5 may, in one or more pairs of two, together with the atoms to which they are bonded, form (un)substituted carbocyclic, heterocyclic group; or R6 and R7 may, together with the atoms to which they are bonded, form (un)substituted carbocyclic, heterocyclic group; Z1 = O, S, CO, etc.; Z2 = H, NO2, halo, etc.; n, p = 0-10 (when m = 0, p is also 0); m = 0-1; q = 1-3], useful as inhibitors of potassium channel function (especially inhibitors of the Kv1 subfamily of voltage gated K+ channels, especially inhibitors Kv1.5 which has been linked to the ultra-rapidly activating delayed rectifier K+ current IKur) in the prevention and treatment of arrhythmia and IKur-associated conditions, were prepared Thus, reacting Me acetoacetate with 2,3-dichlorobenzaldehyde in the presence of piperidine and AcOH in PhMe followed by refluxing the resulting intermediate II with 3-aminopyrazole in 1-propanol afforded the title compound III. The compds. I are effective at 0.001-100 mg/kg/day.

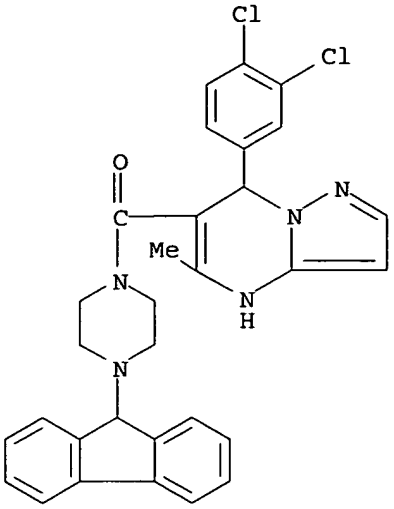
IT **343242-63-7P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyrazolo[1,5-a]pyrimidines as potassium channel inhibitors)

RN 343242-63-7 HCAPLUS

CN Piperazine, 1-[[7-(3,4-dichlorophenyl)-4,7-dihydro-5-methylpyrazolo[1,5-a]pyrimidin-6-yl]carbonyl]-4-(9H-fluoren-9-yl)- (9CI) (CA INDEX NAME)

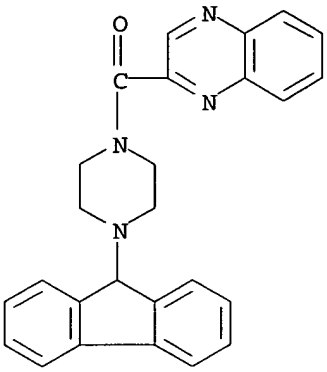


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 10 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:10975 HCAPLUS
DOCUMENT NUMBER: 132:146163
TITLE: Color plates for this article are on pages 51-52. Molecular scaffold-based design and comparison of combinatorial libraries focused on the ATP-binding site of protein kinases
AUTHOR(S): Stahura, Florence L.; Xue, Ling; Godden, Jeffrey W.; Bajorath, Jurgen
CORPORATE SOURCE: Computational Chemistry and Informatics, Bothell, WA, USA
SOURCE: Journal of Molecular Graphics & Modelling (1999), 17(1), 1-9
CODEN: JMGMFI; ISSN: 1093-3263
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Compound libraries were designed to target specifically the ATP cofactor-binding site in protein kinases by combining knowledge- and diversity-based design elements. A key aspect of the approach is the identification of mol. building blocks or scaffolds that are compatible with the binding site and therefore capture some aspects of target specificity. Scaffolds were selected on the basis of docking calcns. and anal. of known inhibitors. We have generated 75 mol. scaffolds and applied different strategies to compute diverse compds. from scaffolds or, alternatively, to screen compound databases for mols. containing these scaffolds. The resulting libraries had a similar degree of mol. diversity, with at most 12% of the compds. being identical. However, their scaffold distributions differed significantly and a small number of scaffolds dominated the majority of compds. in each library.

IT **258282-66-5**
RL: PRP (Properties)
(mol. scaffold-based design and comparison of combinatorial libraries focused on ATP-binding site of protein kinases)
RN 258282-66-5 HCAPLUS
CN Piperazine, 1-(9H-fluoren-9-yl)-4-(2-quinoxalinylcarbonyl)- (9CI) (CA INDEX NAME)

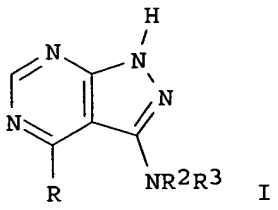


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 11 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:219810 HCAPLUS
DOCUMENT NUMBER: 128:270610
TITLE: Preparation of pyrazolo[3,4-d]-3,4-diamines as epidermal growth factor receptor 2 antagonists
INVENTOR(S): Bold, Guido; Frei, Jorg; Lang, Marc; Traxler, Peter
PATENT ASSIGNEE(S): Novartis A.-G., Switz.; Bold, Guido; Frei, Jorg; Lang, Marc; Traxler, Peter
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9814450	A1	19980409	WO 1997-EP5369		19970930
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2266519	AA	19980409	CA 1997-2266519		19970930
AU 9748642	A1	19980424	AU 1997-48642		19970930
AU 720135	B2	20000525			
EP 929553	A1	19990721	EP 1997-911163		19970930
EP 929553	B1	20050316			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2001501216	T2	20010130	JP 1998-516231		19970930
AT 291022	E	20050415	AT 1997-911163		19970930
US 6251911	B1	20010626	US 1999-269823		19990401
PRIORITY APPLN. INFO.:			CH 1996-2399	A	19961002
			WO 1997-EP5369	W	19970930

OTHER SOURCE(S): MARPAT 128:270610
GI



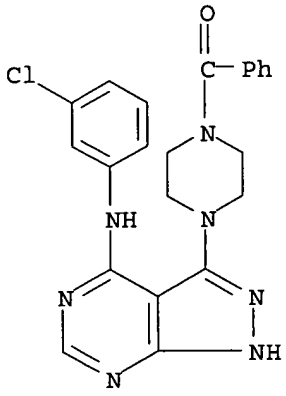
I

AB Title compds. [I; R = NHZR1; R1 = (un)substituted Ph; R2 = H and R3 = COR4,(un)substituted alkyl, C6H4CH2R5, etc.; NR2R3 = heterocyclyl; R4 = alkyl(amino), NHCH2Ph, pyridylmethylamino, Ph, heterocyclyl, etc.; R5 = carboxyalkanoylamino, NHCO2CH2Ph, NHCONH2, etc.; Z = bond, CH2, alkylidene] were prepared Thus, (MeS)2C:C(CN)2 was aminated by PhCH2NH2and the product cyclocondensed with H2NNH2 to give 5-amino-3-benzylamino-1H-pyrazole-4-carbonitrile which was cyclocondensed with 3-ClC6H4NH2 to give I (R = NHC6H4Cl-3, R2 = H)(II; R3 = CH2Ph). The latter was converted in 2 steps to II (R3 = COCMe3). Data for biol. activity of I were given.

IT **205451-86-1P 205451-90-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrazolo[3,4-d]-3,4-diamines as epidermal growth factor receptor 2 antagonists)

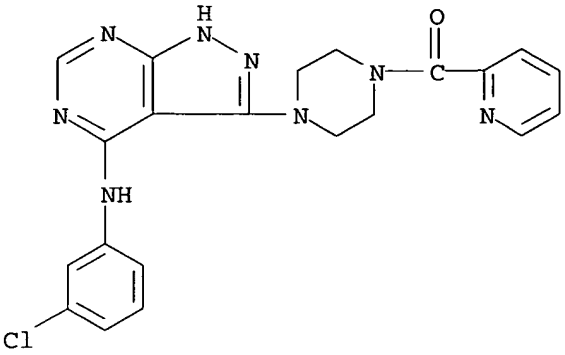
RN 205451-86-1 HCAPLUS

CN Piperazine, 1-benzoyl-4-[4-[(3-chlorophenyl)amino]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]- (9CI) (CA INDEX NAME)



RN 205451-90-7 HCAPLUS

CN Piperazine, 1-[4-[(3-chlorophenyl)amino]-1H-pyrazolo[3,4-d]pyrimidin-3-yl]-4-(2-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 12 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:731037 HCAPLUS
DOCUMENT NUMBER: 127:346754
TITLE: Effect of functional substitutes on the isomerization polymerization of cyclic pseudoureas
AUTHOR(S): Miyamoto, Masatoshi; Shimakura, Masakadzu; Tsutsui, Koji; Aoi, Keigo; Kimura, Yoshiharu
CORPORATE SOURCE: Dep. Polymer Sci. Eng., Faculty Textile Sci., Kyoto Inst. Technol., Kyoto, 606, Japan
SOURCE: Kobunshi Ronbunshu (1997), 54(10), 702-709
CODEN: KBRBA3; ISSN: 0386-2186
PUBLISHER: Kobunshi Gakkai
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

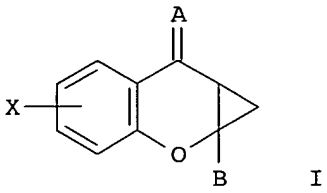
AB Six cyclic pseudoureas having functional substituents were newly prepared, and their ring-opening isomerization polymerization initiated with Me trifluioromethanesulfonate and double isomerization polymerization (DIP) initiated and catalyzed by Me iodide were investigated. The monomers have a common base-structure of 2-(4-substituted piperadin-1-yl)-2-oxazoline (1b-e) or 2-(4-substituted piperidin-1-yl)-2-oxazoline (1f, g). The substituent on the imino ring strongly influenced the polymerization behavior of the monomers in DIP because of their neighboring group participation with the propagating alkyl halide end. The introduction of an aliphatic amide group enhanced the stability of the propagating end, particularly when the substituent was valeroyl (1c), while degradative chain transfer was induced when the substituent was ethoxycarbonyl (1e). The introduction of an ester (1f) or hydroxyl (1g) group caused significant chain transfer in both modes of polymerization

IT **198226-77-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(functional substitute effects on ring-opening isomerization polymerization of piperidinyl oxazoline derivs.)
RN 198226-77-6 HCAPLUS
CN Piperazine, 1-benzoyl-4-(4,5-dihydro-2-oxazolyl)- (9CI) (CA INDEX NAME)

AT 231142	E	20030215	AT 1995-934860		19951020
ES 2191063	T3	20030901	ES 1995-934860		19951020
US 5843988	A	19981201	US 1997-817389		19970418
PRIORITY APPLN. INFO.:			JP 1994-256468	A	19941021
			JP 1995-225365	A	19950901
			WO 1995-JP2163	W	19951020

OTHER SOURCE(S): MARPAT 125:114483

GI



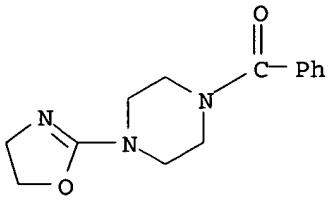
I

AB Novel cyclopropachromenecarboxylate derivs. having a metabolic-regulation type glutamate receptor antagonism and represented by general formula [I; A = oxygen, hydroxyimino, C1-C5 alkyloxyimino or :N-O-(CH2)n-NR1R2 (wherein n = an integer of 2 to 8; R1, R2 = hydrogen or C1-C5 alkyl); B = CO2R3 (wherein R3 = hydrogen or C1-C5 alkyl) or CONR4R5 (wherein R4 and R5 = hydrogen, C1-C5 alkyl, C2-C5 alkenyl, optionally N-substituted C1-C5 aminoalkyl, optionally N-substituted nitrogenous saturated heterocyclic group, Ph substituted by halogen or optionally substituted hydroxyl, 2-pyridyl or C7-C10 aralkyl, or R4 and R5 are combined together to represent an optionally substituted nitrogenous heterocyclic group); X = halo or OR6 (wherein R6 represent hydrogen, C1-C5 alkyl, C3-C6 alkenyl or C7-C10 aralkyl)], and pharmacol. acceptable salts thereof are prepared These compds. are useful for treating and improving brain function- or brain organic disorders-derived diseases (e.g. brain ischemia disorder-derived disorders such as a sequela of brain infarction, brain hemorrhage, or brain arteriosclerosis) or organic disorders-derived various brain diseases such as senile dementia, a sequela of head external trauma or brain surgery, Alzheimer's disease, and Parkinson's disease. Thus, 363 mg trimethylsulfoxonium iodide was added to a suspension of 66 mg NaH in DMF under ice-cooling-cooling, stirred at room temperature for 30 min, treated with 300 mg 2-ethoxycarbonyl-4-oxo-4H-1-benzopyran, and stirred at room temperature for 15 min to give 45% I (X = H, A = O, B = CO2Et). I (X = H, A = :NOH, B = CONHPh) showed IC50 of 3 μM for inhibiting glutamic acid-induced increase in cellular Ca2+ ions in CHO cells expressing rat metabotropic glutamate receptor.

IT **179067-87-9P 179068-19-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopropachromenecarboxylate derivs. having metabotropic glutamate receptor antagonism for treating brain function and/or organic disorders)

RN 179067-87-9 HCAPLUS

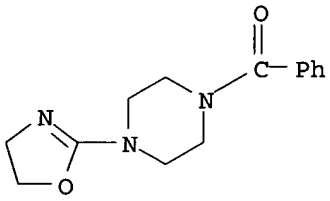
CN Piperazine, 1-(2-benzoxazolyl)-4-[(7,7a-dihydro-7-oxobenzo[b]cyclopropa[e]pyran-1a(1H)-yl)carbonyl]- (9CI) (CA INDEX NAME)



IT **198226-82-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(functional substitute effects on ring-opening isomerization polymerization of
piperidinyl oxazoline derivs.)
RN 198226-82-3 HCAPLUS
CN Piperazine, 1-benzoyl-4-(4,5-dihydro-2-oxazolyl)-, homopolymer (9CI) (CA INDEX NAME)

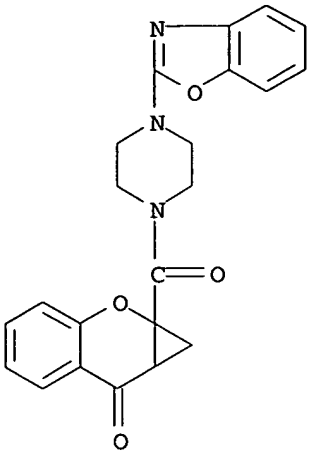
CM 1

CRN 198226-77-6
CMF C14 H17 N3 O2

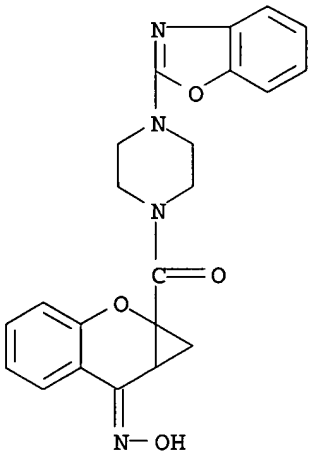


L20 ANSWER 13 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:455865 HCAPLUS
DOCUMENT NUMBER: 125:114483
TITLE: Preparation of cyclopropachromenecarboxylate derivatives having a metabotropic glutamate receptor antagonism
INVENTOR(S): Annoura, Hirokazu; Fukunaga, Atsuko; Tatsuoka, Toshio; Horikawa, Yoshiko
PATENT ASSIGNEE(S): Suntory Limited, Japan
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

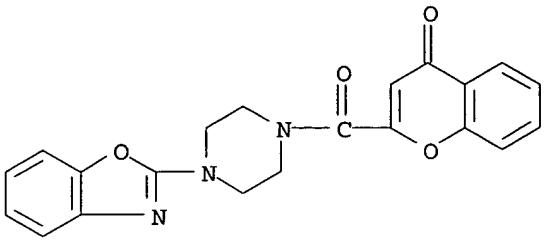
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9612715	A1	19960502	WO 1995-JP2163	19951020
W: US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 08169884	A2	19960702	JP 1995-225365	19950901
EP 787723	A1	19970806	EP 1995-934860	19951020
EP 787723	B1	20030115		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				



RN 179068-19-0 HCAPLUS
CN Piperazine, 1-(2-benzoxazolyl)-4-[[7,7a-dihydro-7-(hydroxyimino)benzo[b]cyclopropa[e]pyran-1a(1H)-yl]carbonyl]- (9CI) (CA INDEX NAME)



IT **179068-49-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclopropachromenecarboxylate derivs. having metabotropic glutamate receptor antagonism for treating brain function and/or organic disorders)
RN 179068-49-6 HCAPLUS
CN Piperazine, 1-(2-benzoxazolyl)-4-[(4-oxo-4H-1-benzopyran-2-yl)carbonyl]- (9CI) (CA INDEX NAME)



L20 ANSWER 14 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:638596 HCAPLUS
DOCUMENT NUMBER: 123:286084
TITLE: Dibenzocycloheptenylidenepiperidine, dibenzocycloheptenylpiperazine, and heterocyclic analogs as PAF antagonists and antihistaminics
INVENTOR(S): Wong, Jesse K.; Piwinski, John J.; Green, Michael J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 29 pp. Cont.-in-part of U.S. Ser. No. 595,329,abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5416087	A	19950516	US 1993-39072	19930407
WO 9206970	A1	19920430	WO 1991-US7170	19911008
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1990-595329 B2 19901010
WO 1991-US7170 W 19911008
OTHER SOURCE(S): MARPAT 123:286084
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

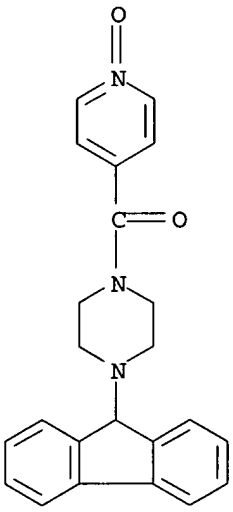
AB Bis-benzo cyclohepta piperidine, piperidylidene and piperazine compds. I [L = N or N+O-, Z = O or S, Y = [C(Ra)2]mX[C(Ra)2]n or II, m and n are integers 0, 1, 2, 3 such that m + n = 0 to 3; when m + n = 1, X = e.g., O, S(O)e where e = 0, 1, or 2; when m + n = 2, X = e.g., O, S(O)e, e = 0-2; when m + n = 3, X = a direct bond; when m + n = 0, X can be any substituent for m + n = 1 and also a direct bond, cyclopropylene, propenylene; each Ra may be the same or different and each independently represents, e.g., H, C1-6-alkyl; the dotted line between the indicated carbon atoms 5 and 6 represents an optional double bond, such that when a double bond is present, A and B each independently represent R11, OR13, halo or OC(O)R11, and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent H2; (OR13)2; (alkyl and H); (alkyl)2; [H and OC(O)R11], (H and OR11); :O or :NOR14; R1, R2, R3, R4 =

e.g., H, halo, CF3; R5, R6 = e.g., H, alkyl, aryl; R7, R8, R9 = e.g., H, halo, CF3; R11 = H, alkyl, aryl; R13 = alkyl, aryl; R14 = H, alkyl; T = CH, C, or N with the dotted line attached to T representing a double bond when T is C and being absent when T is CH or N] and pharmaceutically acceptable salts thereof are disclosed, which possess anti-allergic and/or anti-inflammatory activity. Methods for preparing and using the compds. are also described. Thus, e.g., coupling of 4-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)piperidine (III, preparation given) with isonicotinic acid N-oxide afforded the pyridinylcarbonyl N-oxide derivative IV which demonstrated in vitro PAF antagonism IC50 = 1.2 μM, and in vivo inhibition of PAF-induced bronchospasm in guinea pigs of 82% at 3 mg/kg. Pharmaceutical formulations were given.

IT **142714-92-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(dibenzocycloheptenylidenepiperidine, dibenzocycloheptenylpiperazine, and heterocyclic analogs as PAF antagonists and antihistaminics)

RN 142714-92-9 HCAPLUS

CN Piperazine, 1-(9H-fluoren-9-yl)-4-[(1-oxido-4-pyridinyl)carbonyl]- (9CI) (CA INDEX NAME)



L20 ANSWER 15 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1992:511647 HCAPLUS

DOCUMENT NUMBER: 117:111647

TITLE: Preparation of dibenzocycloheptylidene(pyridinylcarbonyl)piperidine N-oxides and related compounds as platelet-activating factor (PAF) antagonists and antihistamines

INVENTOR(S): Wong, Jesse K.; Piwinski, John J.; Green, Michael J.

PATENT ASSIGNEE(S): Schering Corp., USA

SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

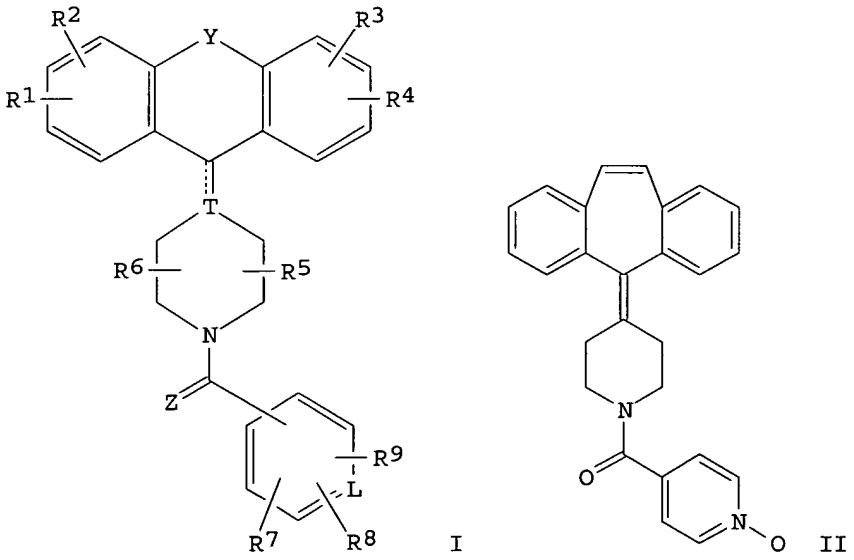
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9206970	A1	19920430	WO 1991-US7170	19911008
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, PL, RO, SD, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
CA 2093646	AA	19920411	CA 1991-2093646	19911008
AU 9188540	A1	19920520	AU 1991-88540	19911008
EP 552245	A1	19930728	EP 1991-918529	19911008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05506249	T2	19930916	JP 1991-517936	19911008
US 5416087	A	19950516	US 1993-39072	19930407
PRIORITY APPLN. INFO.:			US 1990-595329 A2	19901010
			WO 1991-US7170 A	19911008

OTHER SOURCE(S): MARPAT 117:111647

GI



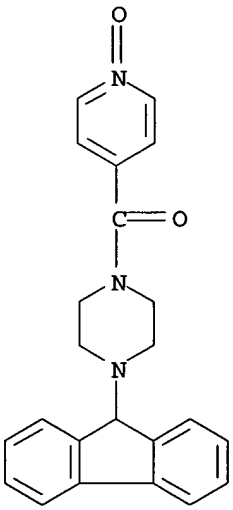
AB The title compds. [I; L = N, N+O-; Z = O, S; Y = (CRa2)mX(CRa2)n, (un)saturated bridge Q; dotted line = optional bond; when bond present then A, B = R11, OR13, halo, etc., when bond absent then A, B = H2, (OR13)2, (alkyl and H), (alkyl)2, etc.; m, n = 0-3, m+n = 0-3; X = O, SO0-2, NR14, CONR14, NR14CO, CSNR14, NR14CS, CO2, O2C, bond, cyclopropylene, propylene, depending on the value of m+n; R14 = H, alkyl; Ra = H, C1-6 alkyl; R1-R4 = H, halo CF3, OR11, NO2, cyano, aryl, (un)substituted alkyl, -alkenyl, etc.; R1R2 = benzo; R3R4 = benzo; R5, R6 = H, aryl, (un)substituted alkyl; R5R6 = O, S; R7-R9 = H, halo, CF3, COR11, SR11, NO2, aryl, etc.; R11 = H, alkyl, aryl; R13 = alkyl, aryl; T = CH, C, N; dotted line attached to T = optional double bond] or their pharmaceutically acceptable salts or

solvates, useful as antiallergics and antiinflammatories, were prepared A solution of 412 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl in 5 mL CH2Cl2 was added dropwise to a mixture of 422 mg 4-(5H-dibenzo[a,d]cyclohept-5-ylidene)piperidine, 234 mg isonicotinic acid N-oxide, and 274 mg 1-hydroxybenzotriazole hydrate in 5 mL CH2Cl2 at -15° under N and the whole allowed to warm to the ambient temp and stirred overnight to give 445 mg title compound II. The latter antagonized PAF-induced human blood platelet aggregation with IC50 = 2 μM, vs. 0.61 μM for the known PAF antagonist 8-chloro-6,11-dihydro-11-(1-acetyl-4-piperidylidene)-5H-benzo[5,6]cyclohepta[1,2-b]pyridine as a pos. control.

IT **142714-92-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as platelet-activating factor antagonist and antihistamine)

RN 142714-92-9 HCAPLUS

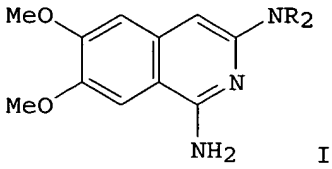
CN Piperazine, 1-(9H-fluoren-9-yl)-4-[(1-oxido-4-pyridinyl)carbonyl]- (9CI) (CA INDEX NAME)



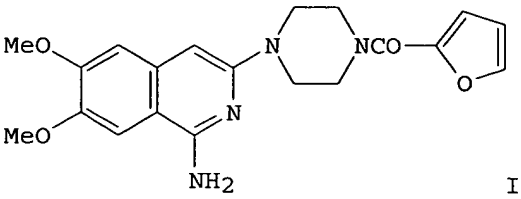
L20 ANSWER 16 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1988:167273 HCAPLUS
DOCUMENT NUMBER:	108:167273
TITLE:	1,3-Diamino-6,7-dimethoxyisoquinoline derivatives as potential α1-adrenoceptor antagonists
AUTHOR(S):	Bordner, Jon; Campbell, Simon F.; Palmer, Michael J.; Tute, Michael S.
CORPORATE SOURCE:	Dep. Discovery Chem., Pfizer Cent. Res., Sandwich/Kent, UK
SOURCE:	Journal of Medicinal Chemistry (1988), 31(5), 1036-9 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 108:167273

GI



II



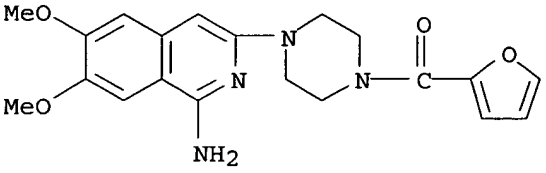
III

AB Treatment of 2,4,5-Me(MeO)2C6H2CN (I) with LiN(CHMe2)2 followed by reaction with R2NCN [R = Me, R2 = (CH2)5] provided 1,3-diamino-6,7-dimethoxyisoquinolines II (R = as above), which were evaluated for α-adrenoceptor binding affinity and antihypertensive activity. II (R = Me) showed no significant affinity for α1-adrenoceptors, while the 3-(2-furoyl-1-piperazinyl) analog III, prepared from I and 1-cyano-4-(tert-butoxycarbonyl)piperazine in 3 steps, was 1000-fold less potent than prazosin. PKa data showed that 34% N(2) protonation of II (R = Me) (pKa = 7.1) would occur at physiol. pH, in agreement with x-ray crystallog. anal. of III.HCl. Comparison of pos. charge distribution following protonation of II (R = Me) with the corresponding quinoline and quinazoline cations confirmed that N(1) protonation is required for these heterocyclic nuclei to bind efficiently to the α1-adrenoceptor. Computer-assisted comparison of the x-ray structures of III.HCl and prazosin suggested that the 4.0 kcal/mol difference in α1-adrenoceptor binding energies was largely due to salt-bridge formation (ca. 3.0 kcal/mol) between the protonated quinazoline and the receptor protein. Neither II nor III were effective antihypertensive agents in rats even when administered at relatively high doses (10 mg/kg). These results support the hypothesis that the antihypertensive activity of prazosin, doxazosin, and related compds. derives solely from α1-adrenoceptor blocking.

IT **113534-00-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and protonation of, with hydrogen chloride)

RN 113534-00-2 HCAPLUS

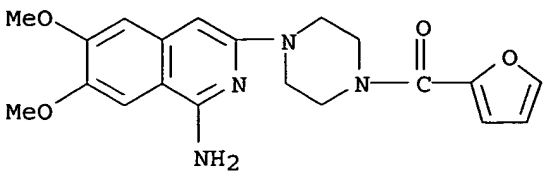
CN Piperazine, 1-(1-amino-6,7-dimethoxy-3-isoquinolinyl)-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)



IT **113533-99-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation, mol. structure, adrenoceptor binding affinity, and antihypertensive activity of)

RN 113533-99-6 HCAPLUS

CN Piperazine, 1-(1-amino-6,7-dimethoxy-3-isoquinolinyl)-4-(2-furanylcarbonyl)-, monohydrochloride (9CI) (CA INDEX NAME)

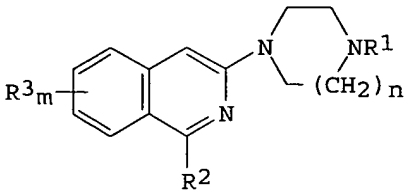


● HCl

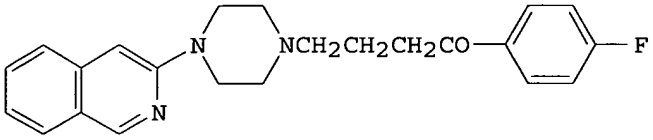
L20 ANSWER 17 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:423646 HCAPLUS
DOCUMENT NUMBER: 97:23646
TITLE: Isoquinoline derivatives, pharmaceutical compositions containing them and their use
INVENTOR(S): Knoz, Elmar; Hock, Franz; Kaiser, Joachim; Kruse, Hansjoerg
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: Eur. Pat. Appl., 27 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 47923	A1	19820324	EP 1981-106884	19810903
EP 47923	B1	19840509		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
DE 3034001	A1	19820422	DE 1980-3034001	19800910
AT 7389	E	19840515	AT 1981-106884	19810903
ES 505191	A1	19820816	ES 1981-505191	19810904
JP 57080372	A2	19820519	JP 1981-139850	19810907
FI 8102783	A	19820311	FI 1981-2783	19810908
FI 71734	B	19861031		
FI 71734	C	19870209		
IL 63765	A1	19850531	IL 1981-63765	19810908
DK 8104006	A	19820311	DK 1981-4006	19810909
NO 8103066	A	19820311	NO 1981-3066	19810909
AU 8175091	A1	19820318	AU 1981-75091	19810909
AU 541976	B2	19850131		
ZA 8106237	A	19820825	ZA 1981-6237	19810909
HU 31176	O	19840428	HU 1981-2595	19810909
HU 187357	B	19851228		
CA 1168232	A1	19840529	CA 1981-385547	19810909
ES 506584	A1	19830301	ES 1981-506584	19811027
ES 506583	A1	19830401	ES 1981-506583	19811027
US 4590273	A	19860520	US 1984-594366	19840328
PRIORITY APPLN. INFO.:			DE 1980-3034001 A	19800910
			EP 1981-106884 A	19810903
			US 1981-300434 A2	19810908

OTHER SOURCE(S): CASREACT 97:23646
GI



I



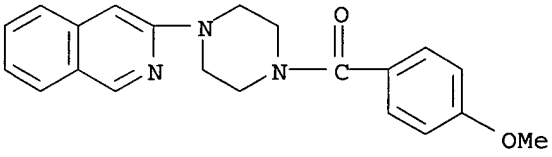
II

AB I [R1 = H, C1-6 alkyl, C1-4 alkoxy, C3-6 cycloalkyl, thienyl, furyl, pyridyl, aryl, (CH2)pCOR (R = aryl, furyl, thienyl, pyridyl; p = 0-4), etc.; R2 = H, C1-6 alkyl; R3 = H, halo, C1-6 alkyl, alkoxy, etc.; m, n = 1, 2] were prepared as antiarrhythmics, antihypertensives, and neuroleptics (no data). Thus, 3-chloroisoquinline and pyrazine gave 3-pyrazinoisoquinoline, which with ω-chloro-4-florobutyrophenone ethylene ketal (followed by deprotection) gave II.

IT **82117-68-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 82117-68-8 HCAPLUS

CN Piperazine, 1-(3-isoquinolinyl)-4-(4-methoxybenzoyl)- (9CI) (CA INDEX NAME)

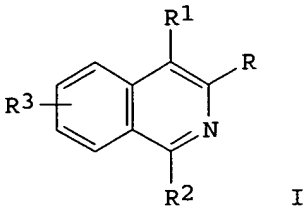


L20 ANSWER 18 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1981:587098 HCAPLUS
DOCUMENT NUMBER: 95:187098
TITLE: Isoquinoline derivatives and their use for medicaments
INVENTOR(S): Bartmann, Wilhelm; Konz, Elmar; Kruse, Hansjoerg; Geyer, Harry M.
PATENT ASSIGNEE(S): Hoechst A.-G. , Fed. Rep. Ger.
SOURCE: U.S., 17 pp. Cont.-in-part of U.S. Ser. No. 20,411, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4282223	A	19810804	US 1979-76862	19790919
DE 2811312	A1	19790927	DE 1978-2811312	19780316
PRIORITY APPLN. INFO.:			DE 1978-2811312 A	19780316

GI



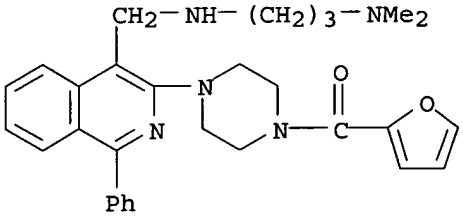
I

AB Antidepressant (no data) isoquinolines I (R = amino; R1 = CO2H, cyano, CHO, CH2OH, alkoxymethyl, aminoalkoxymethyl, acyloxymethyl, aminomethyl, carbamoyl, aminoalkoxycarbonyl, optionally substituted vinyl; R2 = optionally substituted Ph, pyridyl, thienyl; R3 = H, halogen, OH, alkyl, alkoxy, NO2, NH2, OCH2Ph, OCH2O, OCH2CH2O) were prepared Thus 20 g I (R = Cl, R1 = CHO, R2 = Ph, R3 = H) was treated with 15 g N-methylpiperazine to give 21 g I (R = N-methylpiperazino, R1 = CHO, R2 = Ph, R3 = H).

IT **72128-11-1P 72128-12-2P 79602-14-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 72128-11-1 HCAPLUS

CN Piperazine, 1-[4-[[[3-(dimethylamino)propyl]amino]methyl]-1-phenyl-3-isoquinolinyl]-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)

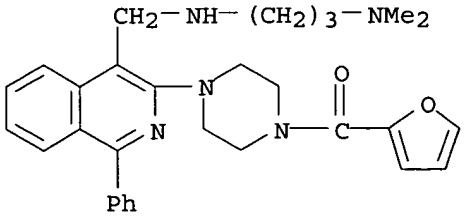


RN 72128-12-2 HCAPLUS

CN Piperazine, 1-[4-[[[3-(dimethylamino)propyl]amino]methyl]-1-phenyl-3-isoquinolinyl]-4-(2-furanylcarbonyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

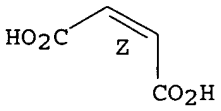
CRN 72128-11-1
CMF C30 H35 N5 O2



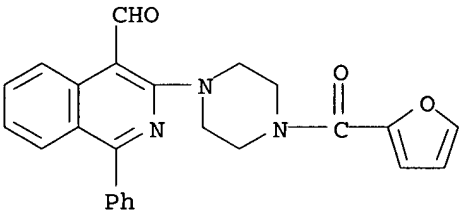
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



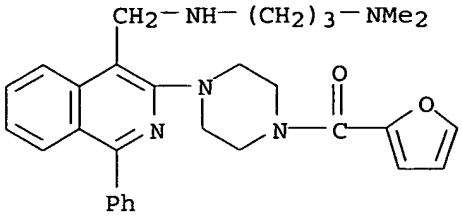
RN 79602-14-5 HCAPLUS
CN Piperazine, 1-(4-formyl-1-phenyl-3-isoquinolinyl)-4-(2-furanylcarbonyl)-
(9CI) (CA INDEX NAME)



L20 ANSWER 19 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:6430 HCAPLUS
DOCUMENT NUMBER: 92:6430
TITLE: Isoquinoline derivatives
INVENTOR(S): Bartmann, Wilhelm; Konz, Elmar; Kruse, Hansjoerg; Geyer, Harry Maurice
PATENT ASSIGNEE(S): Hoechst A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 55 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2811312	A1	19790927	DE 1978-2811312	19780316
EP 4332	A1	19791003	EP 1979-100737	19790312
EP 4332	B1	19810826		
R: CH, DE, FR, GB				
US 4282223	A	19810804	US 1979-76862	19790919
PRIORITY APPLN. INFO.:			DE 1978-2811312	19780316
			US 1979-20411 A2	19790314

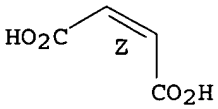
GI



CM 2

CRN 110-16-7
CMF C4 H4 O4

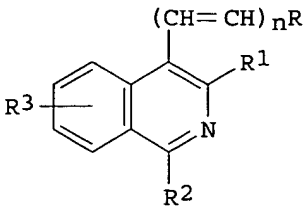
Double bond geometry as shown.



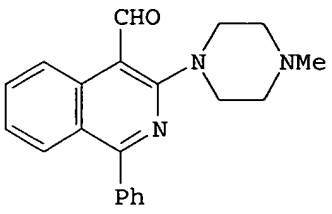
L20 ANSWER 20 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:560166 HCAPLUS
DOCUMENT NUMBER: 85:160166
TITLE: Piperazinyl quinazoline bronchodilators
INVENTOR(S): Cronin, Timothy H.; Hess, Hans J. E.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 8 pp. Division of U.S. 3,914,423.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3966936	A	19760629	US 1975-581830	19750529
US 3723434	A	19730327	US 1970-55964	19700717
US 3814760	A	19740604	US 1972-315617	19721215
US 3914423	A	19751021	US 1974-444669	19740221
PRIORITY APPLN. INFO.:			US 1970-55964 A3	19700717
			US 1972-315617 A3	19721215
			US 1974-444669 A3	19740221

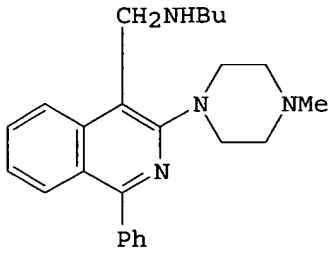
GI



I



II



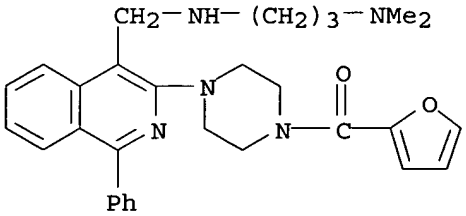
III

AB A series of .apprx.100 I, in most of which n = 0 or 1, R = CHO, CH2OH, or substituted amino or amide, R1 = substituted amino, R2 = aryl, R3 = H, 6-Cl, or 6,7-(methylenedioxy) were prepared as sedatives and muscle relaxants (no data). Thus 3-chloro-1-phenyl-4-iosquinolinecarboxaldehyde was treated with 1-methylpiperazine to give II. Also prepared was, e.g., III.

IT **72128-11-1P 72128-12-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 72128-11-1 HCAPLUS

CN Piperazine, 1-[4-[[[3-(dimethylamino)propyl]amino]methyl]-1-phenyl-3-isoquinolinyl]-4-(2-furanylcarbonyl)- (9CI) (CA INDEX NAME)

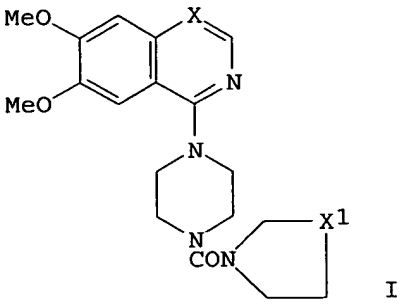


RN 72128-12-2 HCAPLUS

CN Piperazine, 1-[4-[[[3-(dimethylamino)propyl]amino]methyl]-1-phenyl-3-isoquinolinyl]-4-(2-furanylcarbonyl)-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72128-11-1
CMF C30 H35 N5 O2



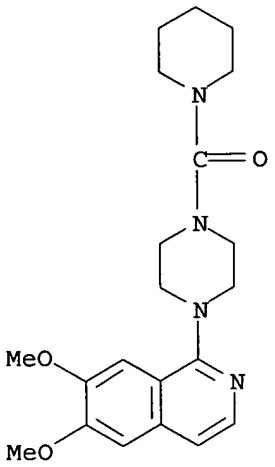
I

AB Amides I [X = N, X1 = CH2CH2, CH(OH)CH2; X = CH, X1 = CH2CH2, CHOH, CH(OH)CH2, CH2CH(OH), CH2CMe(OH)] were prepared by treating the piperazinylquinazoline or piperazinylisoquinoline with COCl2 and amidation of the carbonyl chlorides. I at 60 mg/kg orally gave 27-59% protection against histamine-induced bronchostriction in guinea pigs.

IT **41647-77-2P 41647-79-4P 41647-80-7P 41647-81-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bronchodilating activity of)

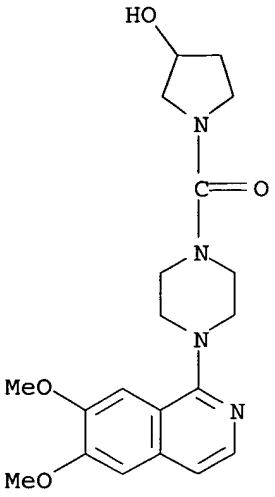
RN 41647-77-2 HCAPLUS

CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)- (9CI) (CA INDEX NAME)

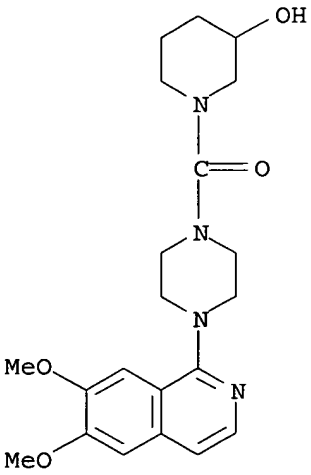


RN 41647-79-4 HCAPLUS

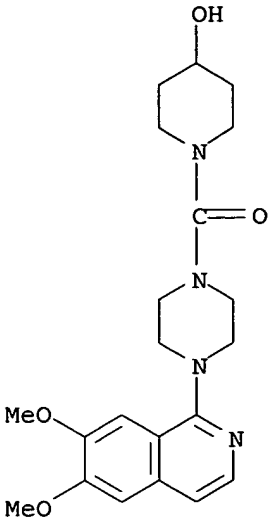
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-pyrrolidinyl)carbonyl]- (9CI) (CA INDEX NAME)



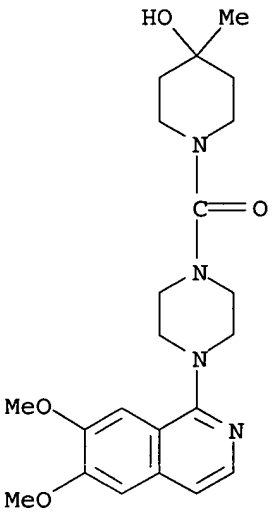
RN 41647-80-7 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 41647-81-8 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



IT **41647-82-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 41647-82-9 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-4-methyl-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



L20 ANSWER 21 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:44155 HCAPLUS
DOCUMENT NUMBER: 84:44155
TITLE: Quinazoline and isoquinoline bronchodilators
INVENTOR(S): Cronin, Timothy H.; Hess, Hans J. E.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 8 pp. Division of U.S. 3,814,760.
CODEN: USXXAM
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

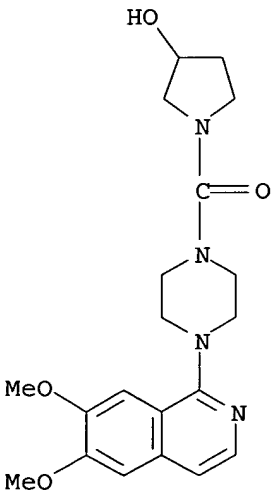
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3914423	A	19751021	US 1974-444669	19740221
US 3723434	A	19730327	US 1970-55964	19700717
US 3814760	A	19740604	US 1972-315617	19721215
US 3966936	A	19760629	US 1975-581830	19750529
PRIORITY APPLN. INFO.:			US 1970-55964 A3	19700717
			US 1972-315617 A3	19721215
			US 1974-444669 A3	19740221

GI For diagram(s), see printed CA Issue.

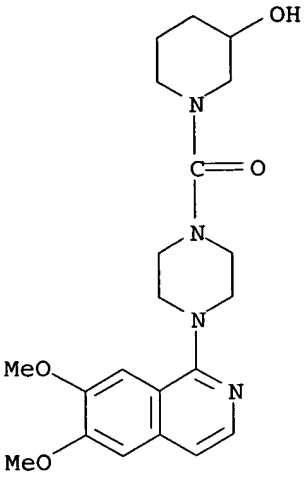
AB Piperazines I [X = CH, RR1 = (CH2)5, CH2CH(OH)CH2CH2, CH2CH(OH)(CH2)3, (CH2CH2)2CHOH, (CH2CH2)2CMeOH; X = N, RR1 = (CH2)5, CH2CH(OH)(CH2)3] were prepared by treating the N-substituted piperazines with COCl2 and the amines. I gave 27-59% protection against histamine-induced bronchial constriction in guinea pigs at 60 mg/kg orally.

IT **41647-79-4P 41647-80-7P 41647-81-8P**
41647-82-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and bronchodilator activity of)

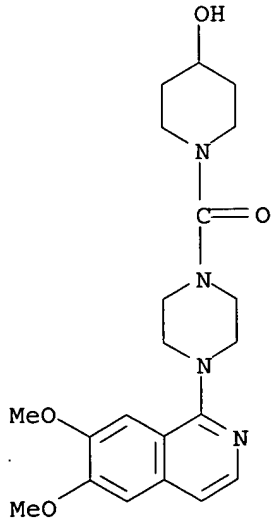
RN 41647-79-4 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-pyrrolidinyl)carbonyl]- (9CI) (CA INDEX NAME)



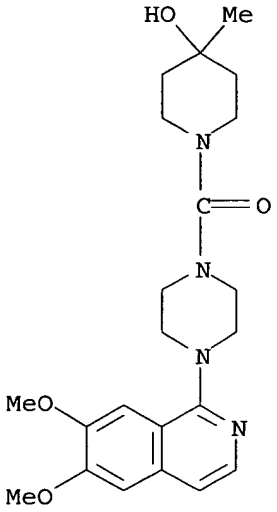
RN 41647-80-7 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



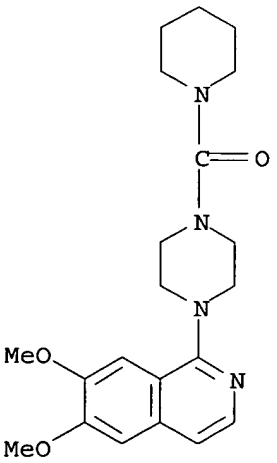
RN 41647-81-8 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 41647-82-9 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-4-methyl-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)

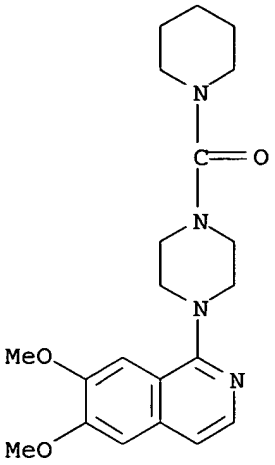


IT **41647-73-8P 41647-77-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 41647-73-8 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)-, hydrochloride (9CI) (CA INDEX NAME)



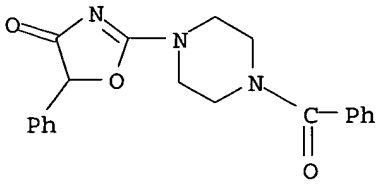
●x HCl

RN 41647-77-2 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)- (9CI) (CA INDEX NAME)

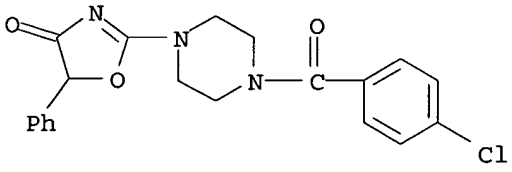


L20 ANSWER 22 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:601749 HCAPLUS
DOCUMENT NUMBER: 83:201749
TITLE: Antimalarials. Synthesis and antimalarial activity of 1-(4-methoxycinnamoyl)-4-(5-phenyl-4-oxo-2-oxazolin-2-yl)piperazine and derivatives
AUTHOR(S): Herrin, Thomas R.; Pauvlik, Jeanne M.; Schuber, Evelyn V.; Geiszler, Adolph O.
CORPORATE SOURCE: Div. Antibiot. Nat. Prod., Abbott Lab., North Chicago, IL, USA
SOURCE: Journal of Medicinal Chemistry (1975), 18(12), 1216-23
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 83:201749
GI For diagram(s), see printed CA Issue.
AB The preparation and activity against Plasmodium berghei of analogs of 1-(4-methoxycinnamoyl)-4-(5-phenyl-4-oxo-2-oxazolin-2-yl)piperazine (I) [51314-69-3] are described. Replacement of the cinnamoyl group was accomplished by acylation or alkylation of 1-(5-phenyl-4-oxo-2-oxazolin-2-yl)piperazine [14021-76-2]. Modifications of the 5-phenyl group were prepared either by a sequence of reactions involving mandelic ester-pemoline-piperazine pemoline or by the reaction of 5-aryl-2-thio-2,4-oxazolidinedione with piperazine [110-85-0] or N-substituted piperazines. In a similar manner pemoline [2152-34-3] was allowed to react with N-arylpiperazine, hexahydro-1H-1,4-diazepine [505-66-8], and 2,6-dimethylpiperazine [108-49-6] to provide N-arylpiperazine pemoline derivs. and variations in the piperazine moiety. Several compds. in which the 2-oxazolin-4-one ring was replaced with other heterocyclic rings were prepared as were several open-chain analogs. Six compds. (3 of them substituted in the para position of the 5-phenyl group, 1 with changes in the cinnamoyl group and substitution on the 5-phenyl group, and 2 N-arylpiperazine pemoline derivs.) were found to be active against Plasmodium berghei.
IT **57260-19-2P 57260-20-5P 57260-23-8P**
57260-26-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and antimalarial activity of)

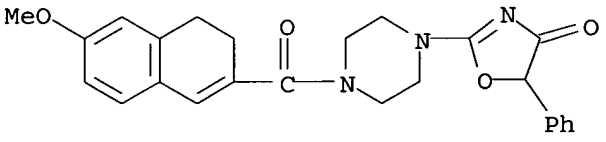
RN 57260-19-2 HCAPLUS
CN Piperazine, 1-benzoyl-4-(4,5-dihydro-4-oxo-5-phenyl-2-oxazolyl)- (9CI) (CA INDEX NAME)



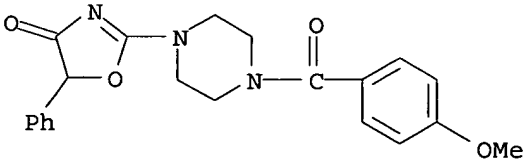
RN 57260-20-5 HCAPLUS
CN Piperazine, 1-(4-chlorobenzoyl)-4-(4,5-dihydro-4-oxo-5-phenyl-2-oxazolyl)- (9CI) (CA INDEX NAME)



RN 57260-23-8 HCAPLUS
CN Piperazine, 1-[(3,4-dihydro-6-methoxy-2-naphthalenyl)carbonyl]-4-(4,5-dihydro-4-oxo-5-phenyl-2-oxazolyl)- (9CI) (CA INDEX NAME)



RN 57260-26-1 HCAPLUS
CN Piperazine, 1-(4,5-dihydro-4-oxo-5-phenyl-2-oxazolyl)-4-(4-methoxybenzoyl)- (9CI) (CA INDEX NAME)



L20 ANSWER 23 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1974:505553 HCAPLUS
DOCUMENT NUMBER: 81:105553
TITLE: Piperazino quinazoline bronchodilators
INVENTOR(S): Cronin, Timothy H.; Hess, Hans J. E.
PATENT ASSIGNEE(S): Pfizer Inc.
SOURCE: U.S., 6 pp. Division of U.S. 3,723,434 (CA

78;159657b).
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

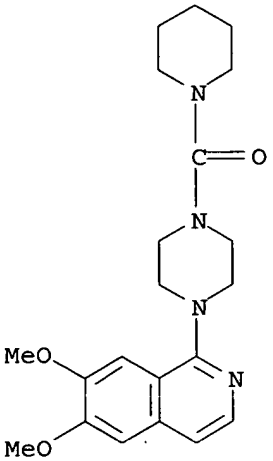
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 3814760	A	19740604	US 1972-315617		19721215
US 3723434	A	19730327	US 1970-55964		19700717
US 3914423	A	19751021	US 1974-444669		19740221
US 3966936	A	19760629	US 1975-581830		19750529
PRIORITY APPLN. INFO.:			US 1970-55964	A3	19700717
			US 1972-315617	A3	19721215
			US 1974-444669	A3	19740221

GI For diagram(s), see printed CA Issue.

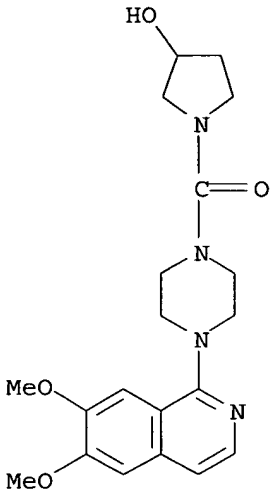
AB The piperazinoquinoazolines I (R = piperidino, 3-hydroxypiperidino) and isoquinolines II (R = piperidino, 3-hydroxy-1-pyrrolidinyl, 3- and 4-hydroxypiperidino, 4-methyl-4-hydroxypiperidino) were prepared Thus, 4-piperazinyl-6,7-dimethoxyquinazoline was treated with COCl2 followed by piperidine to give I (R = piperidino). At 60 mg/kg II (R = piperidino) was a bronchodilator.

IT **41647-77-2P 41647-79-4P 41647-80-7P**
41647-81-8P 41647-82-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

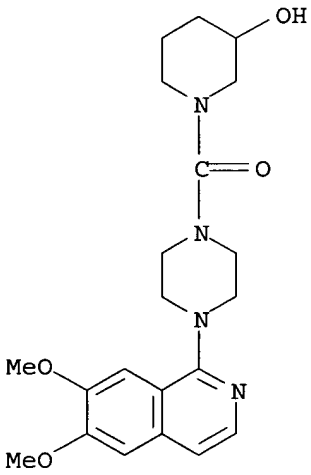
RN 41647-77-2 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)- (9CI) (CA INDEX NAME)



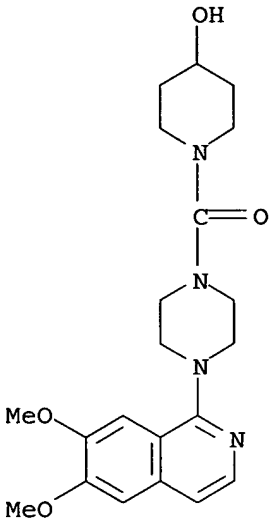
RN 41647-79-4 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-pyrrolidinyl)carbonyl]- (9CI) (CA INDEX NAME)



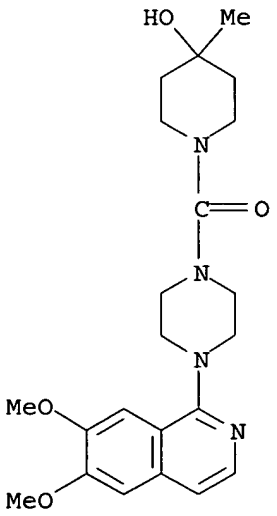
RN 41647-80-7 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 41647-81-8 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 41647-82-9 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-4-methyl-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



L20 ANSWER 24 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:159657 HCAPLUS
DOCUMENT NUMBER: 78:159657
TITLE: Piperazino isoquinoline bronchodilators
INVENTOR(S): Cronin, Timothy H.; Hess, Hans Jurgen E.
PATENT ASSIGNEE(S): Pfizer Inc.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3723434	A	19730327	US 1970-55964	19700717
GB 1277566	A	19720614	GB 1970-1277566	19701013
US 3814760	A	19740604	US 1972-315617	19721215
US 3914423	A	19751021	US 1974-444669	19740221
US 3966936	A	19760629	US 1975-581830	19750529

PRIORITY APPLN. INFO.:

US 1970-55964	A	19700717
US 1972-315617	A3	19721215
US 1974-444669	A3	19740221

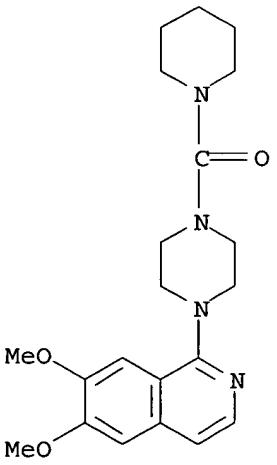
GI For diagram(s), see printed CA Issue.

AB 4-Piperazinyl-6,7-dimethoxyquinazoline was treated with Cl2CO to give the piperazinylquinazoline I (R = Cl), which was treated with piperidine to give I (R = piperidino). The piperazinylsoquinoline II (R = piperidino) (III) was similarly prepared I and II (R = 3-hydroxypiperidino, 3-hydroxy-1-pyrrolidinyl) were similarly prepared III was also prepared from 1-(piperidino-carbonyl)piperazine and 1-chloro-6,7-dimethoxyisoquinoline. At 60 mg/kg II were bronchodilators.

IT **41647-73-8P 41647-77-2P 41647-79-4P**
41647-80-7P 41647-81-8P 41647-82-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 41647-73-8 HCAPLUS

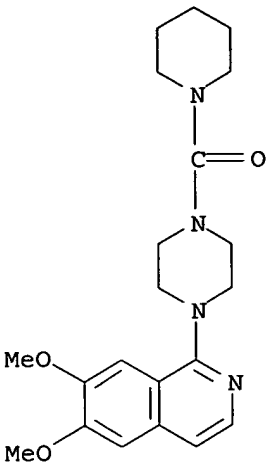
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)-, hydrochloride (9CI) (CA INDEX NAME)



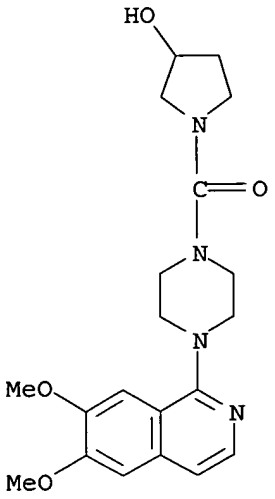
●x HCl

RN 41647-77-2 HCAPLUS

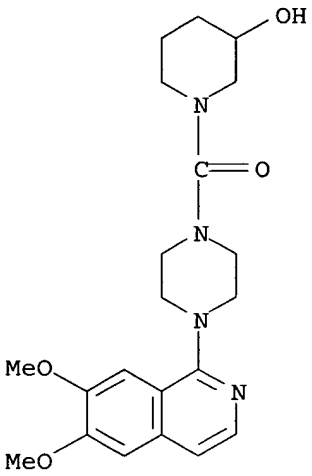
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-(1-piperidinylcarbonyl)- (9CI) (CA INDEX NAME)



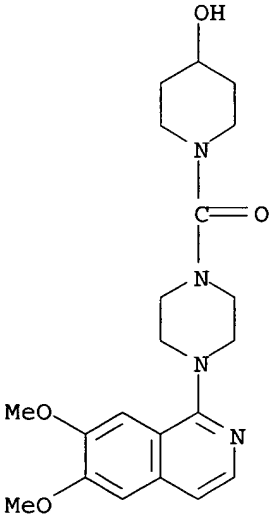
RN 41647-79-4 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-pyrrolidinyl)carbonyl]- (9CI) (CA INDEX NAME)



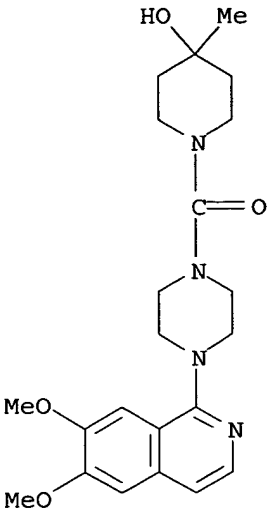
RN 41647-80-7 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(3-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



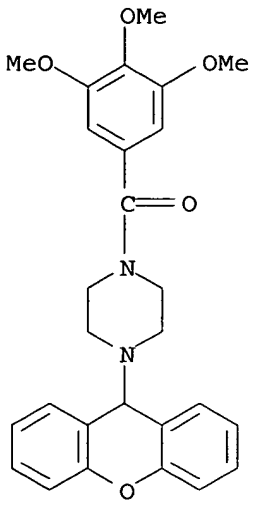
RN 41647-81-8 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



RN 41647-82-9 HCAPLUS
CN Piperazine, 1-(6,7-dimethoxy-1-isoquinolinyl)-4-[(4-hydroxy-4-methyl-1-piperidinyl)carbonyl]- (9CI) (CA INDEX NAME)



L20 ANSWER 25 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:3796 HCAPLUS
DOCUMENT NUMBER: 76:3796
TITLE: Piperazine derivatives. III. Diethylcarbamyl and xanthene derivatives
AUTHOR(S): Toldy, Lajos; Toth, Istvan; Borsy, Jozsef; Andrasi, Ferenc
CORPORATE SOURCE: Inst. Med. Res., Budapest, Hung.
SOURCE: Acta Chimica Academiae Scientiarum Hungaricae (1971), 70(1-2), 101-22
CODEN: ACASA2; ISSN: 0001-5407
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB Substituted piperazines were prepared as anticholinergic agents for treating ulcers. Of 66 compds. prepared the 1-(9-xanthenecarbonyl)-4-[β-(4-alkyl-1-piperazinyl)ethyl]piperazines (I) [especially I (R = iso-Bu)] showed the best peroral resorption. In an example, 12.4 g 1-diethylcarbamoyl-4-(β-chloroethyl)piperazine was stirred for 3 hr at 130° with 22.12 g N-diethylcarbamoylpiperazine. The mixture was cooled, worked up, dissolved in MeOH and treated with alc. HCl to give 9.8 g II. Nineteen I (R = alkyl, CO2Et, Et2NCO, substituted aryl, CO2CH2Ph) were prepared analogously.
IT **17558-16-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 17558-16-6 HCAPLUS
CN Piperazine, 1-(3,4,5-trimethoxybenzoyl)-4-(9H-xanthen-9-yl)- (9CI) (CA INDEX NAME)



L20 ANSWER 26 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:95853 HCAPLUS
DOCUMENT NUMBER: 68:95853
TITLE: Derivatives of 2-amino-4-oxazolinone useful in therapeutic compositions
INVENTOR(S): Aron-Samuel, Jan M. D.
SOURCE: Brit., 12 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1085922		19671004	GB	19650510

GI For diagram(s), see printed CA Issue.

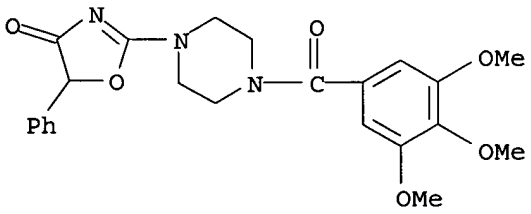
AB Preparation of the title derivs., useful as antiinflammatory, antipyretic, and analgesic agents, is described. Thus, a mixture of 35.2 g. I (R = Ph, R1 = R2 = H) and 81 g. pyrrolidine was refluxed 1.5 hrs. to give 24 g. I (R = Ph, NR1R2 = 1-pyrrolidinyl), m. 150-2°. Other I were prepared similarly (R, NR1R2, and m.p. given): Ph, piperidino, 125°; Ph, 1-piperazinyl, 146-8°; Ph, 4-methyl-1-piperazinyl, 148-50°; Ph, 4-(3,4,5-trimethoxybenzoyl)-1-piperazinyl, 250-2°; Bu, piperidino, - (HCl salt m. 134-6°); hexyl, piperidino, - (HCl salt m. 124-6°); hexyl, 4-butyl-1-piperazinyl, 48-50°; hexyl, 4-methyl-1-piperazinyl, 40° (HCl salt m. 208°); Bu, morpholino, 90°; Bu, 4-(hydroxyethyl)-1-piperazinyl, 71°; Bu, 4-(p-tolyl)-1-piperazinyl, 139°; iso-Bu, piperidino, 64-6°; hexyl, 4-methylpiperidino, - (HCl salt m. 138-40°); Bu, 1-pyrrolidinyl, - (HCl salt m. 153°); hexyl, 1-pyrrolidinyl, 101°; hexyl, 4-(p-tolyl)-1-piperazinyl, 132°; hexyl, 4-(hydroxyethyl)-1-piperazinyl, 86°; iso-Bu, 4-methyl-1-piperazino, - (HCl salt m. 258-60°); Ph, 4-phenyl-1-piperazinyl, 190-2°; Ph, 4-(p-tolyl)-1-piperazinyl, 180°; Ph, morpholino, 164-6°; Me, 4-methyl-1-piperazinyl, - (HCl salt m. 243°); p-FC6H4, 4-methyl-1-piperazinyl, 156°; Ph, 4-benzyl-1-piperazinyl, 162-4°; p-BrC6H4, 4-methyl-1-piperazinyl, 182-4°; Ph,

4-(hydroxyethyl)-1-piperazinyl, 90-2°; Ph, 4-(p-methoxyphenyl)-1-piperazinyl, 182-4°; Ph, 4-(p-chlorophenyl)-1-piperazinyl, 156-8°; p-MeOC6H4, piperidino, 108-10°; o-ClC6H4, piperidino, 98-100°; 3,4-methylenedioxyphenyl, 1-pyrrolidinyl, 152-4°; Ph, 4-methylpiperidino, 104-6°; Ph, 3-methylpiperidino, 136-8°; Me, piperidino, 48-50°; p-ClC6H4, piperidino, 118-20°; p-BrC6H4, piperidino, 138-40°; Ph, 4-acetyl-1-piperazinyl, 142-4°; p-BrC6H4, morpholino, 180-2°; p-ClC6H4, 4-(p-tolyl)-1-piperazinyl, 202-4°; Ph, 4-(diethylaminoethyl)-1-piperazinyl, 84-6°; Ph, 3-methyl-4-acetyl-1-piperazinyl, 162-4°; Ph, 3,5-dimethyl-4-acetyl-1-piperazinyl, 180-90°; Ph, 4-propyl-1-piperazinyl, 134-6°; Ph, 4-butyl-1-piperazinyl, 112-14°; Pr, piperidino, - (HCl salt m. 124-6°); hexyl, 4-propyl-1-piperazinyl, 44-5°; hexyl, 1-piperazinyl, 78°; hexyl, 4-(diethylaminoethyl)-1-piperazinyl, 35-6°; Ph, 4-(4'-chlorobutyrophenon-4-yl)-1-piperazinyl, 152-4°; Ph, 4-(4'-fluorobutyrophenon-4-yl)-1-piperazinyl, 134-6°; tetradecyl, piperidino, 64-6°; tetradecyl, 4-methyl-1-piperazinyl, 74-6°; nonyl, piperidino, 45°; nonyl, 4-methyl-1-piperazinyl, 54-6°; p-FC6H4, piperidino, 98-100°; Bu, 4-methyl-1-piperazinyl, - (HCl salt m. 216-17°; Bu, 4-methyl-1-piperazinyl, 56-7°; Bu, 4-propyl-1-piperazinyl, 64-6°; Bu, 4-phenyl-1-piperazinyl, 118°. Acute toxicity, antiinflammatory effect, analgesic effect, and antipyretic action of these compds. is given.

IT **14021-77-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 14021-77-3 HCAPLUS

CN Piperazine, 1-(4-oxo-5-phenyl-2-oxazolin-2-yl)-4-(3,4,5-trimethoxybenzoyl)- (8CI) (CA INDEX NAME)



L20 ANSWER 27 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:13001 HCAPLUS
DOCUMENT NUMBER: 68:13001
TITLE: Piperazine derivatives
INVENTOR(S): Toldy, Lajos; Toth, Istvan; Borsy, Jozsef; Polgari, Istvan
PATENT ASSIGNEE(S): Gyogyszerkutato Intezet
SOURCE: Hung., 10 pp.
CODEN: HUXXAT
DOCUMENT TYPE: Patent
LANGUAGE: Hungarian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

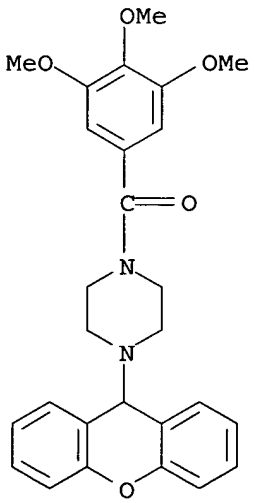
HU 153832 19670722 HU 19651116

AB A solution of 28.4 g. 9-chloroxanthene in 144 ml. absolute PhMe was added with stirring to a solution of 25 g. 1-(o-methylbenzyl)piperazine in 150 ml. absolute PhMe and 19 ml. Et3N at reflux temperature in 1 hr. and the mixture refluxed 9 hrs., filtered, washed with NaHCO3 solution and H2O, and worked up to yield 1-(9-xanthenyl)-4-(o-methylbenzyl)piperazine, m. 134-6° (C6H6-hexane 1:1). Similarly were obtained 1-(9-xanthenyl)-4-(2-hydroxyethyl)piperazine, m. 128-9° (C6H6-hexane) [3,4,5-trimethoxybenzoate m. 134-5° (C6H6-hexane, EtOH)], 1-(9-xanthenyl)-4-(3-chloro-6-pyridazinyl)piperazine, m. 216-18° (C6H6-hexane), 1-(9-xanthenyl)-4-(diethylcarbamoyl)piperazine, m. 124-6° (C6H6-hexane), 1-(9-xanthenyl)-4-(3,4,5-trimethoxybenzoyl)piperazine, m. 145-7° (C6H6-hexane, EtOH), and 1,4-bis(9-xanthenyl)piperazine, m. 143-5° (EtOH, C6H6-hexane). A mixture of 10 g. xanthydrol, 11 g. 1-benzyloxycarbonylpiperazine, 60 ml. absolute PhMe, and 3.3 ml. AcOH was refluxed 18 hrs and the H2O formed in the reaction was removed continuously by azeotropic distillation to yield 1-(9-xanthenyl)-4-benzyloxycarbonylpiperazine, m. 153-4° (C6H6-hexane). 1-(9-Xanthenyl)-4-(β-phenylisopropyl)piperazine, m. 110-12° (Me2CO), and 1-(9-xanthenyl)-4-[α-(2-pyridyl)ethyl]piperazine, m. 134-5° (Me2CO), were prepared analogously.

IT **17558-16-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 17558-16-6 HCAPLUS

CN Piperazine, 1-(3,4,5-trimethoxybenzoyl)-4-(9H-xanthen-9-yl)- (9CI) (CA INDEX NAME)



L20 ANSWER 28 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1967:95027 HCAPLUS

DOCUMENT NUMBER: 66:95027

TITLE: Substituted i-amino-4-oxazolinones

INVENTOR(S): Aron-Samuel, Jan M. D.

SOURCE: Neth. Appl., 20 pp.
CODEN: NAXXAN

DOCUMENT TYPE: Patent

LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

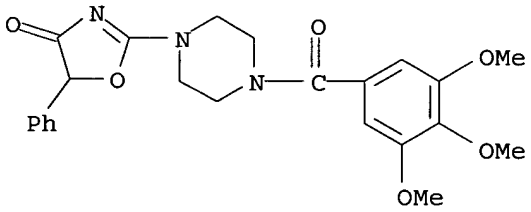
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 6606319		19661111		
DE 1645909			DE	
FR 5458			FR	
US 3567826		19710000	US	
PRIORITY APPLN. INFO.:			GB	19650510

GI For diagram(s), see printed CA Issue.

AB I, in which R' is a piperidino, pyrrolidino, morpholino, or piperazino ring, are prepared by the reaction of 1 part I (R' = NH2) (II) with 5-10 parts of a heterocyclic base. II are prepared by the reaction of RCH(OH)CO2R2 with guanidine. Thus to prepare II (R = Bu) (III) a mixture of Et α-hydroxycaproate and 59 g. guanidine in EtOH is refluxed 1.5 hrs. to give 33% III, m. 217-19°. Thus, are also prepared II (R and m.p. given): iso-Bu, 203°; hexyl, 212-14°; nonyl, 198-200°; tetradecyl, 180-2°. To prepare I (R = Bu, R1 = piperidino) (IV) a mixture of 6 g. III and 38 ml. piperidine is refluxed 20 min., after which the excess piperidine is removed. The residue is dissolved in 25 ml. Et2O, and HCl added to give 85% IV.HCl, m. 134-6°. The LD50 determined by oral administration to mice is 520 mg./kg. Thus are also prepared I (R, R1, m.p., and LD50 in mg./kg. given): iso-Bu, piperidino, 64-6°, 1000; hexyl, 4-methylpiperidino, 138-40°, 1400; Bu, pyrrolidino, 153° (as HCl salt), 1250; hexyl, pyrrolidino, 101°, 800; hexyl, N-(p-tolyl)piperazino, 132°, 1500; hexyl, N-(hydroxyethyl)piperazino, 86°, 1500; iso-Bu, N-methylpiperazino, 258-60° (HCl-salt), 2000; Ph, piperidino, 125°, 600; Ph, N-methylpiperazino, 148-50°, 350; Ph, N-phenylpiperazino, 190-2°, 4000; Ph, pyrrolidino, 152°, 500; Ph, N-p-tolylpiperazino, 180°, 4000 (V); Ph, morpholino, 164-6°; 3500; Me, N-methylpiperazino, 243° (HCl salt), 450; p-fluorophenyl, N-methylpiperazino, 156°, 650; Ph, N-benzylpiperazino, 162-4°, 4000; p-bromophenyl, N-methylpiperazino, 182-4°, -; Ph, N-(hydroxyethyl)piperazino, 90-2°, 800; Ph, N-(p-methoxyphenyl)piperazino, 182-4°, 3000; Ph, N-(p-chlorophenyl)piperazino, 156-8°, 4000; p-methoxyphenyl, piperidino, 108-10°, -; o-chlorophenyl, piperidino, 98-100°, -; 3,4-methylenedioxyphenyl, pyrrolidino, 152-4°, -; Ph, 4-methylpiperidino, 104-6°, 1000; Ph, 3-methylpiperidino, 136-8°, 1200; Me, piperidino, 48-50°, 2250; Ph, piperazino, 146-8°, 115; Ph, 4-(3,4,5-trimethoxybenzoyl)piperazino, 250-2°, 4000; p-chlorophenyl, piperidino, 118-20°, 3500; p-bromophenyl, piperidino, 138-40°, 4000; Ph, N-acetylpiperazino, 142-4°, -; p-bromophenyl, morpholino, 180-2°, -; p-chlorophenyl, N-p-tolylpiperazino, 202-4°, -; Ph, N-diethylaminoethylpiperazino, 84-6°, -; Ph, 3-methy-N-acetylpiperazino, 162-4°, -; Ph, 3,5-dimethyl-N-acetylpiperazino, 180-90°, -; Ph, N-propylpiperazino, 134-6°, -; Ph, N-butylpiperazino, 112-14°, -; Pr, piperidino, 124-6° (HCl salt), -; hexyl, N-butylpiperazino, 48-50°, -; hexyl, N-propylpiperazino, 44-5°, -; hexyl, piperazino, 78°, -; hexyl, N-diethylaminoethylpiperazino, 35-6°, -; Ph, N-(4-fluorobutyrophenon-4-yl)piperazino, 134-6°, 800; Bu, N-(p-tolyl)piperazino, 139°, 1500; Bu, N-(hydroxyethyl)piperazino, 71°, 800; Ph, N-(4-chlorobutyrophenon-4-yl)piperazino, 152-4°, -; Bu, morpholino, 90°, 1500; tetradecyl, piperidino, 64-6°, 800; tetradecyl, N-methylpiperazino,

74-6°, 800; nonyl, piperidino, 45°, 800; nonyl, N-methylpiperazino, 54-6°, 800; p-fluorophenyl, piperidino, 98-100°, 600; hexyl, piperidino, 124-6° (HCl salt), 1400; Bu, N-methylpiperazino, 56-7°, 650; hexyl, N-methylpiperazino, 40°, 1200 (VI); Bu, N-propylpiperazino, 64-6°, 400; Bu, N-phenylpiperazino, 118°, 800. These compds., especially V and VI, have inflammation combating, febrifugal, and sedative properties and are therefore useful for the treatment of rheumatism.

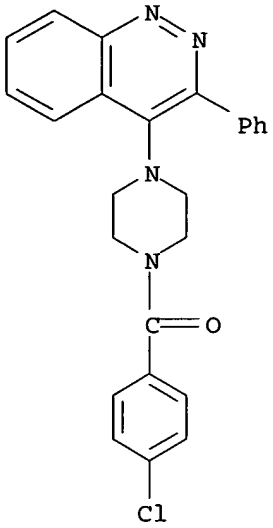
IT **14021-77-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 14021-77-3 HCAPLUS
CN Piperazine, 1-(4-oxo-5-phenyl-2-oxazolin-2-yl)-4-(3,4,5-trimethoxybenzoyl)- (8CI) (CA INDEX NAME)



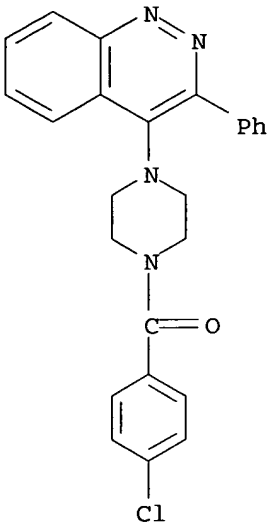
L20 ANSWER 29 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:465520 HCAPLUS
DOCUMENT NUMBER: 65:65520
ORIGINAL REFERENCE NO.: 65:12203b-c
TITLE: Synthesis of potential antineoplastic agents. XV. Some 1,4-bisamides of 1,2,3,4-tetrahydroquinoxaline
AUTHOR(S): Schuyler, Peter; Popp, Frank D.; Noble, Adria Catala; Alwani, Dru W.; Masters, Barry R.
CORPORATE SOURCE: Clarkson Coll. of Technol., Potsdam, NY
SOURCE: Journal of Medicinal Chemistry (1966), 9(5), 704-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB cf. CA 65, 5459c. A number of Cl-containing and unsatd. 1,4-bisamides have been prepared from 1,2,3,4-tetrahydroquinoxaline and from substituted 1,2,3,4-tetrahydroquinoxalines. Although many of these amides are active against KB cell culture, they are inactive against animal tumors. A number of related amides were also prepared from 1,2,3,4-tetrahydroquinoline and 1,2,3,4-tetrahydroisoquinoline.

IT **10579-38-1**, Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)-
(preparation of)
RN 10579-38-1 HCAPLUS
CN Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)- (7CI, 8CI) (CA INDEX NAME)



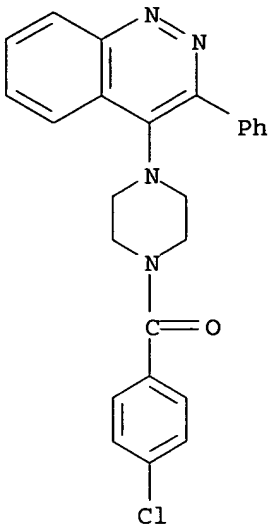
L20 ANSWER 30 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:465519 HCAPLUS
DOCUMENT NUMBER: 65:65519
ORIGINAL REFERENCE NO.: 65:12203b
TITLE: 3-Phenylcinnolines. II. Preparation of 4-amino derivatives
AUTHOR(S): Lowrie, Harman S.
CORPORATE SOURCE: Div. of Chem. Res., G. D. Searle & Co., Chicago
SOURCE: Journal of Medicinal Chemistry (1966), 9(5), 670-4
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. preceding abstract The development of methods for converting 3-phenylcinnoline-4-carboxylic acids into the 4-hydroxy and 4-chloro analogs led to the preparation of 4-amino compds. which were examined for pharmacol. activity. 27 references.
IT **10579-38-1**, Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)-
(preparation of)
RN 10579-38-1 HCAPLUS
CN Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)- (7CI, 8CI) (CA INDEX NAME)



L20 ANSWER 31 OF 31 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:465518 HCAPLUS
DOCUMENT NUMBER: 65:65518
ORIGINAL REFERENCE NO.: 65:12203a-b
TITLE: 3-Phenylcinnolines. I. Some reactions and derivatives of 3-phenylcinnoline-4-carboxylic acids
AUTHOR(S): Lowrie, Harman S.
CORPORATE SOURCE: Div. of Chem. Res., G. D. Searle & Co., Chicago
SOURCE: Journal of Medicinal Chemistry (1966), 9(5), 664-9
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 65:65518

AB A series of amide, hydrazide, and ester derivs. of the title acids and 2 phenylbutazone analogs of 3-phenylcinnoline were prepared These were examined for pharmacol. activity. 21 references.

IT **10579-38-1**, Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)-
(preparation of)
RN 10579-38-1 HCAPLUS
CN Piperazine, 1-(p-chlorobenzoyl)-4-(3-phenyl-4-cinnolinyl)- (7CI, 8CI) (CA INDEX NAME)

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L23            30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 NOT L20


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=> d ibib abs l23 1-30

L23  ANSWER 1 OF 30  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:141028  HCAPLUS
DOCUMENT NUMBER:          142:240315
TITLE:                    Preparation of indolyl-3-glyoxylic acid amides for the
                          treatment of tumors
INVENTOR(S):              Gerlach, Matthias; Schuster, Tilmann;
                          Schmidt, Peter; Baasner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S):       Zentaris G.m.b.H., Germany
SOURCE:                   PCT Int. Appl., 25 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.        DATE
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WO 2005014542	A2	20050217	WO 2004-EP7573	20040709
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RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10334040	A1	20050310	DE 2003-10334040	20030725
PRIORITY APPLN. INFO.:			DE 2003-10334040 A	20030725

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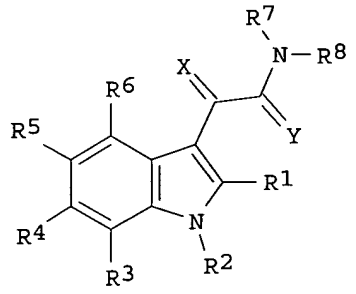

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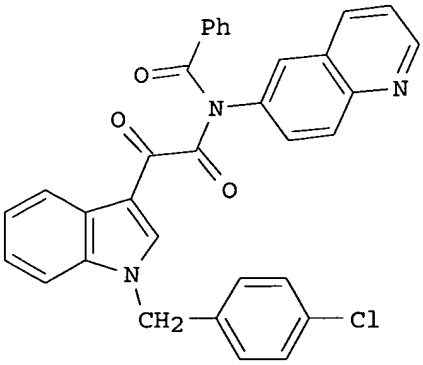

II

AB Title compds. I [R1, R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, aryl, etc.;R7 = SO2X1, COX2, COOX3, etc.; X1 = N(alkyl)2, OH, (un)substituted alkyl, etc.; X2 = (un)substituted aryl, heteroaryl, alkylaryl, etc.; X3 = (un)substituted cycloalkyl, heterocyclyl, aryl, etc.; R8 = Het; X = O, S with provisos; Y = O, S] and their pharmaceutically acceptable salts were prepared In human cervical cancer cell line (KB/HeLa) antiproliferative assay, indolylglyoxylic acid amide II exhibited an IC50 value of 0.170 μg/mL. Compds. I are claimed to be useful for the treatment of tumors.

L23 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:78242 HCAPLUS
DOCUMENT NUMBER: 142:176683
TITLE: Preparation of N-substituted indolyl-3-glyoxylamides as antitumor agents
INVENTOR(S): **Gerlach, Matthias**; Schuster, Tilmann; Schmidt, Peter; Baasner, Silke; Gunther, Eckhard
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005020636	A1	20050127	US 2004-892040		20040715
PRIORITY APPLN. INFO.:			US 2003-490004P	P	20030725

OTHER SOURCE(S): MARPAT 142:176683
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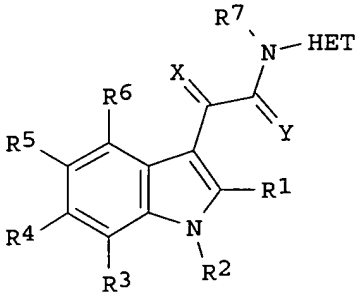

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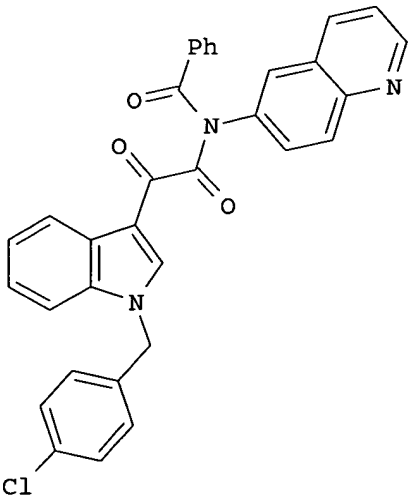

II

AB The title compds. I [R1, R3-R6 = H, (un)substituted (cyclo)alkyl, (hetero)aryl, alkylaryl, etc.; R2 = (un)substituted alkyl, alkylaryl, alkylheteroaryl; R7 = SO2X1 (wherein X1 = dialkylamino, OH, (un)substituted (cyclo)alkyl, (hetero)aryl, etc.), COX2 (X2 = (un)substituted (hetero)aryl, alkylaryl, alkylheteroaryl), etc.; X = O, S or geminally linked H and OH; Y = O, S; HET = (un)saturated or aromatic heterocycle comprising N, O and S which can be bonded to the amide nitrogen directly or via alkyl bridge], useful as medicaments, in particular for the treatment of tumors, were prepared General procedure for synthesis of compds. I such as II which comprises reacting 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-quinolin-6-ylacetamide with acyl chloride, was described. The compound II was tested for inhibition of selected tumor cell lines and antiproliferative action on MDR tumor cell lines (data given). The pharmaceutical composition comprising the compound I is disclosed.

L23 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:74111 HCAPLUS
DOCUMENT NUMBER: 142:176867
TITLE: Preparation of acridinyl piperazinyl methanones and related compounds as anticancer drugs.
INVENTOR(S): **Gerlach, Matthias**; Emig, Peter; Paulini, Klaus; Czech, Michael; Schuster, Tilmann; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007643	A1	20050127	WO 2004-EP7020	20040629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10331500	A1	20050224	DE 2003-10331500	20030711

PRIORITY APPLN. INFO.: DE 2003-10331500 A 20030711
OTHER SOURCE(S): MARPAT 142:176867
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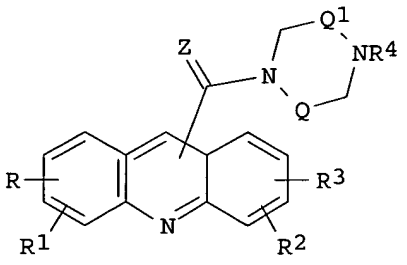

I

AB Title compds. [I; Z = O, S; m, n = 0-4; R-R3 = H, OH, OR5; R4 = (substituted) aryl, aralkyl, heteroaryl, heteroaralkyl; R5 = acyl; Q = (CH2)m; Q1 = (CH2)n], were prepared Thus, glutaric acid mono-[3-[4-(acridin-9-carbonyl)piperazin-1-yl]phenyl]ester showed EC50 = 0.01 μg/mL against KB/HeLa cells in an XTT proliferation assay.
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:53490 HCAPLUS
DOCUMENT NUMBER: 142:309180
TITLE: Design and synthesis of a focused library of novel

aryl- and heteroaryl-ketopiperazides

AUTHOR(S): **Gerlach, Matthias**; Claus, Eckhard; Baasner, Siike; Mueller, Gilbert; Polymeropoulos, Emmanuel; Schmidt, Peter; Guenther, Eckhard; Engel, Juergen

CORPORATE SOURCE: Drug Discovery, Zentaris GmbH, Frankfurt am Main, Germany

SOURCE: Archiv der Pharmazie (Weinheim, Germany) (2004), 337(12), 695-703
CODEN: ARPMAS; ISSN: 0365-6233

PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1-Phenyl-4-piperazinyl-carbonyl-substituted nitrogen-containing heterocycles were discovered at Zentaris as a new class of potent, synthetic, small mol. tubulin inhibitors with strong antiproliferative activity. The lead structure of this class, D-24203, proved to be a potent inhibitor of in vivo tumor growth in different xenograft models including mammary and renal cancers. As part of our efforts in the lead optimization process to expand structural diversity as well as to optimize bioavailability parameters such as solubility and metabolic stability for these compds., we produced and evaluated a focused library containing 320 compds. Five new heterocyclic compound classes with comparable activity properties in the cytotoxicity and tubulin polymerization assay could be identified. In silico calculated bioavailability parameters for selected library members provides new compound classes with improved solubility properties. Library design, development of adequate solution phase methodol., and synthesis will be presented, as well as results of lead optimization.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:34599 HCAPLUS

DOCUMENT NUMBER: 142:134620

TITLE: Preparation of acridine derivatives as antitumor agents

INVENTOR(S): **Gerlach, Matthias**; Emig, Peter; Paulini, Klaus; Czech, Michael; Schuster, Tilman; Gunther, Eckhard

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 21 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005009809	A1	20050113	US 2004-879280		20040629
PRIORITY APPLN. INFO.:			US 2003-486525P	P	20030711

OTHER SOURCE(S): MARPAT 142:134620

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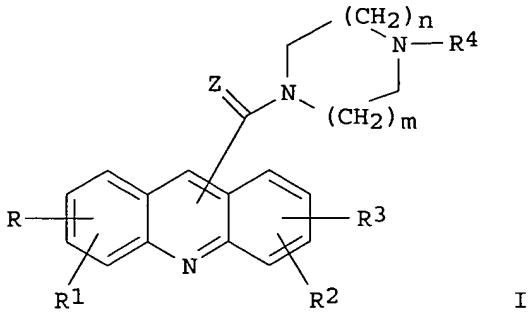

I

AB The invention relates to (heterocyclylcarbonyl)acridine derivs. of the formula (I) [Z = O, S; n, m = 0-4; R, R1, R2, R3 may optionally be attached to the heteroarom. carbon atoms C1 to C9 of the acridine, are identical or different and independently of one another are H, HO or OR5, but the radicals R, R1, R2 and R3 are not simultaneously H; R4 = C6-14 aryl, C6-14 aryl-C1-4 alkyl, C2-10 heteroaryl or C2-10 heteroaryl-C1-4 alkyl containing one or more heteroatoms selected from the group consisting of N, O and S, where the C1-4 alkyl radical may be unsubstituted or mono or polysubstituted; or, if R, R1, R2, R3 may optionally be attached to the heteroarom. carbon atoms C1 to C9 of the acridine, are identical or different and independently of one another and are H, straight-chain or branched C1-8 alkyl, C3-7 cycloalkyl, straight-chain or branched C1-8 alkylcarbonyl, HO, straight-chain or branched C1-8 alkoxy, halogen, straight-chain or branched aryl-C1-8 alkoxy, trityloxy, trimethylsilyloxy, amino, mono(C1-4 alkyl)amino, di(C1-4 alkyl)amino, (C2-5 cycloalkyl)amino, morpholino, etc.; R5 = -SO2-X1 (where X1 = NMe2, hydroxy, alkoxy, etc.), C(O)-X2 (where X2 = (un)substituted alkyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl, etc.), etc.] or physiol. acceptable salts thereof. These compds. are useful for treating benign and malignant tumors in humans and mammals. Thus, 6.66 g (11.06 mmol) polymer-bound N-benzyl-N-cyclohexylcarbodiimide (1.66 mmol/g) was added to a solution of 1.8 g (7.05 mmol) 1,3-dihydroxyacridine-9-carboxylic acid in 40 mL DMF. The mixture was heated at 60° and allowed to react for 30 min, treated with 1.03 g (5.64 mmol) 1-(6-methyl-2-pyridinyl)piperazine, and allowed to react for a further 4 h to give, after workup and silica gel chromatog., 2.3 g (1,3-dihydroxyacridin-9-yl)[4-(6-methylpyridin-2-yl)piperazin-1-yl]methanone (74.8%). The compds. I inhibited the proliferation of human tumor cell lines such as human cervical carcinoma cell line KB/Hela, ovarian adenocarcinoma cell line SKOV3, human glioblastoma cell line SF-268, and lung carcinoma cell line NCI-H460 with EC50 of 0.007-0.293 μg/mL. Six compds. I were also tested for inhibiting the polymerization of tubulin and exhibited EC50 of 1.08-4.82.

L23 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1080885 HCAPLUS
DOCUMENT NUMBER: 142:56172
TITLE: Preparation of 1-(4-chlorobenzyl)indoles as tubulin polymerization inhibitors with apoptosis inducing activity
INVENTOR(S): **Gerlach, Matthias**; Schuster, Tilmann; Emig, Peter; Schmidt, Peter; Bassner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108702	A1	20041216	WO 2004-EP5593	20040525
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EP 1484329	A1	20041208	EP 2003-12868	20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:		
US 2003-476277P	P	20030605
EP 2003-12868	A	20030606
EP 2004-11598	A	20040515

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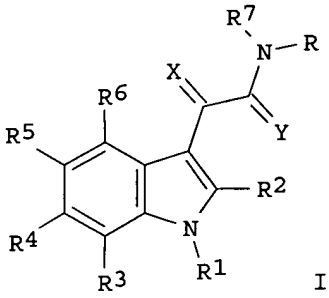

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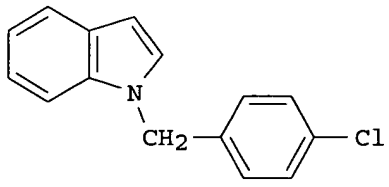

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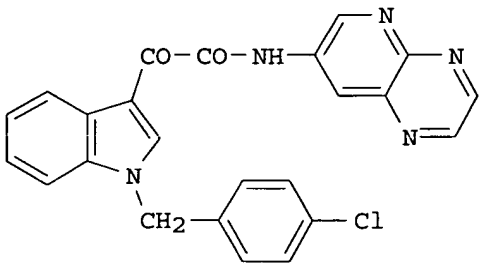

III

AB Title comounds I [R = (un)substituted heterocycle containing N, O, S heteroatoms; R1 = (un)substituted alkyl-aryl; R2 = H, (un)substituted alkyl; R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, etc.; R7 = alkylcarbonyl, alkoxycarbonyl; X, Y = S, O] and their pharmaceutically acceptable salts were prepared For example, oxalyl chloride acylation of

chlorobenzylindole II, i.e., prepared from indole and 4-chlorobenzyl chloride, followed by pyrido[2,3-b]pyrazin-7-amine amidation afforded claimed chlorobenzylindole III in 68% yield. In human tubulin polymerization inhibition assays, 4-examples of compds. I exhibited EC50 values ranging from 0.71-1.26 μg/mL, i.e., the EC50 value of chlorobenzylindole III was 0.71 μg/mL. Compds. I are claimed to be useful as antitumor agents.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:1054280 HCAPLUS
DOCUMENT NUMBER: 142:38145
TITLE: Preparation of 1-(4-chlorobenzyl)indoles as tubulin polymerization inhibitors with apoptosis inducing activity
INVENTOR(S): Emig, Peter; **Gerlach, Matthias**; Paulini, Klaus; Czech, Michael; Schuster, Tilmann; Schmidt, Peter; Baasner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1484329	A1	20041208	EP 2003-12868		20030606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
WO 2004108702	A1	20041216	WO 2004-EP5593		20040525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2004266762	A1	20041230	US 2004-858751		20040602

PRIORITY APPLN. INFO.:			
	US 2003-476277P	P	20030605
	EP 2003-12868	A	20030606
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	EP 2004-11598	A	20040515
	US 2004-572025P	P	20040517

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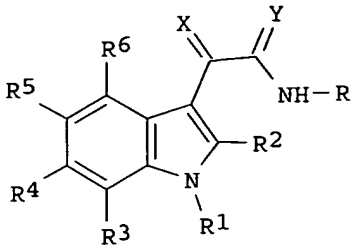

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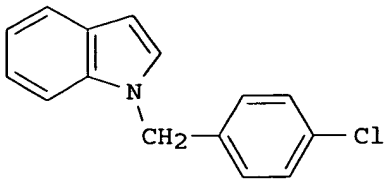

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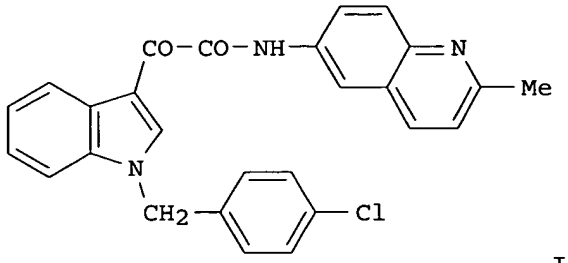


III

AB Title comounds I [R = (un)substituted quinolyl, pyridopyrazinyl, indazolyl; R1 = alkyl-aryl; R2 = H; R3, R4, R5, R6 = H, (un)substituted alkyl, cycloalkyl, etc.; X, Y = S, O] and their pharmaceutically acceptable salts were prepared For example, oxalyl chloride acylation of chlorobenzylindole II, i.e., prepared from indole and 4-chlorobenzyl chloride, followed by 6-amino-2-methylquinoline amidiation afforded claimed chlorobenzylindole III in 77% yield. In human tubulin polymerization inhibition assays, 6-examples of compds. I exhibited EC50 values ranging from 0.71-1.27 μg/mL, i.e., the EC50 value of chlorobenzylindole III was 1.16 μg/mL. Compds. I are claimed to be useful as antitumor agents.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:678789 HCAPLUS

DOCUMENT NUMBER: 141:182364

TITLE: (+)-(1R,5S,6R)-1-[3-(9,9-Dimethyl-4,4-dioxo-4λ6-thiatricyclo[6.1.1.02,6]-dec-2-en-5-yl)-2-tert-butyldimethylsilyloxy-4,6-dimethoxyphenyl]-3-methylbutan-1-one methyl tert-butyl ether solvate at 133 K

AUTHOR(S): Bats, Jan W.; Berger, Bernd; **Gerlach, Matthias**; Reggelin, Michael

CORPORATE SOURCE: Institut fuer Organische Chemie, Universitaet Frankfurt, Frankfurt am Main, D-60439, Germany

SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1999), C55(2), ii, IUC9900002
CODEN: ACSCEE; ISSN: 0108-2701
URL: http://journals,iucr.org/c/issues/1999/05/02/issconts.html

PUBLISHER: Munksgaard International Publishers Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure determination of the title compound was undertaken to establish the

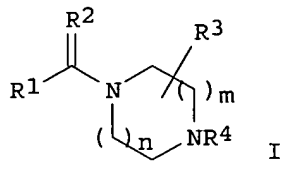
absolute configuration of the chiral centers. Crystals of the compound are orthorhombic, space group P212121, with a 13.129(3), b 19.201(4), c 27.672(6), c 27.672(6) Å; Z = 4 (2 mols./Z), dc = 1.156; R = 0.061, Rw(F2) = 0.114 for 13,583 reflections. The 2 independent mols. have very similar conformations. The solvent mol. is not involved in short intermol. contacts.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:20666 HCAPLUS
DOCUMENT NUMBER: 140:77166
TITLE: Preparation of arylcarbonylpiperazines and heteroarylcarbonylpiperazines for treating benign and malignant tumor diseases
INVENTOR(S): Emig, Peter; **Gerlach, Matthias**; Polymeropoulos, Emmanuel; Mueller, Gilbert; Schmidt, Peter; Baasner, Silke; Guenther, Eckhard
PATENT ASSIGNEE(S): Zentaris Gmbh, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004002965	A1	20040108	WO 2003-EP6555		20030620
W: AU, BR, BY, CA, CN, CO, GE, HR, HU, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, UA, UZ, YU, ZA					
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
EP 1517898	A1	20050330	EP 2003-761482		20030620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003012294	A	20050412	BR 2003-12294		20030620
CA 2433983	AA	20031229	CA 2003-2433983		20030627
US 2004097734	A1	20040520	US 2003-608520		20030627
ZA 2004009610	A	20050418	ZA 2004-9610		20041126
PRIORITY APPLN. INFO.:			US 2002-393027P	P	20020629
			WO 2003-EP6555	W	20030620

OTHER SOURCE(S): MARPAT 140:77166
GI



I

AB Title compds. [I; R1 = (substituted) fluoren-9-one, isoxazolyl, cinnolinyl, isothiazolyl, isoquinolinyl, 9H-fluorenyl, 9H-xanthenyl, 1H-pyrazolyl; R2 = O, S; R3 = H, (substituted) alkyl, halo, CO2H, CONH2; R4 = (substituted) (hetero)aryl, alkylaryl, alkylhetaryl; m, n = 0-3],

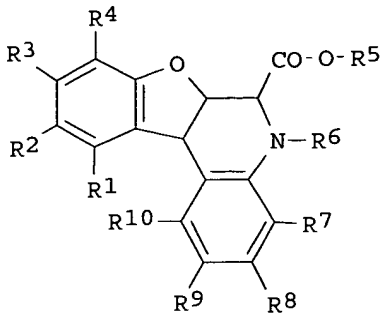
were prepared Thus, 9-fluorenone-4-carbonyl chloride in DMF was successively treated with N-methylmorpholine, 1-(3,5-dimethoxyphenyl)piperazine, and 1-benzotriazolyltripyrrolidinophosphonium hexafluorophosphate followed by stirring for 12 h at room temperature to give 79,3% 4-[4-(3,5-dimethoxyphenyl)piperazine-1-carbonyl]fluoren-9-one. The latter inhibited proliferation in XTT cytotoxicity test in human tumor cells with EC50 = 0,2-0,555 μg/mL.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:133277 HCAPLUS
DOCUMENT NUMBER: 138:170088
TITLE: Preparation of 5,6,6a,11b-tetrahydro-7-oxa-5-aza-benzo[c]fluoren-6-carboxylic acids as NMDA antagonists for the treatment of pain
INVENTOR(S): **Gerlach, Matthias**; Przewosny, Michael; Englberger, Werner Guenter; Reissmueller, Elke; Bloms-Funke, Petra; Maul, Corinna; Jagusch, Utz-Peter
PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014124	A1	20030220	WO 2002-EP8886	20020805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10137487	A1	20030327	DE 2001-10137487	20010803
CA 2456124	AA	20030220	CA 2002-2456124	20020805
EP 1412361	A1	20040428	EP 2002-764838	20020805
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011734	A	20040921	BR 2002-11734	20020805
JP 2005500374	T2	20050106	JP 2003-519073	20020805
NZ 531372	A	20050324	NZ 2002-531372	20020805
US 2004248889	A1	20041209	US 2004-770126	20040203
ZA 2004001725	A	20050131	ZA 2004-1725	20040302
PRIORITY APPLN. INFO.:			DE 2001-10137487 A	20010803
			WO 2002-EP8886 W	20020805

OTHER SOURCE(S): CASREACT 138:170088; MARPAT 138:170088
GI



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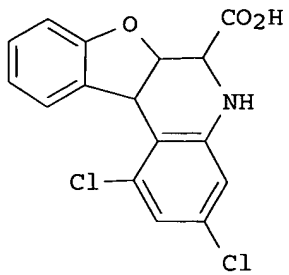


II

AB Title compds. I [R1, R2, R3, R4 = H, halo, CN, etc.; R5 = H, alkyl, alkenyl, etc.; R6 = R12, ZR12; R12 = H, alkyl, alkenyl, etc.; Z = (un)substituted alkyl, alkenyl, alkynyl; R7, R8, R9, R10 = H, halo, CN, etc.] and their pharmaceutically acceptable salts were prepared For example, acid catalyzed three-component coupling of benzofuran, oxoacetic acid and 3,5-dichlorobenzenamine provided claimed benzo[c]fluorene II (no data provided). In glycine binding site studies of the NMDA receptor channel, one specific example of compound I, benzo[c]fluorene II exhibited a Ki = 0.053 μM. Compds. I are claimed useful as analgesic agents for the treatment of pain.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:716280 HCAPLUS
DOCUMENT NUMBER: 137:232666
TITLE: Preparation of pyrazolopyrimidines and thiazolopyrimidines as inhibitors and/or stimulators of nucleoside transport proteins
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna; Jagusch, Utz-Peter; Sundermann, Bernd; Fuhr, Martin; IJzerman, Adriaan P.; Dissen-De Groote, Miriam
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany; Universiteit Leiden
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072585	A2	20020919	WO 2002-EP2722	20020313
WO 2002072585	A3	20030220		

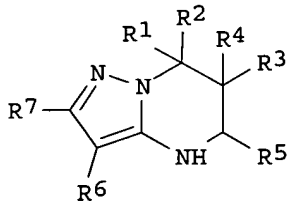
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10112197	A1	20020919	DE 2001-10112197	20010314
DE 10153344	A1	20030515	DE 2001-10153344	20011029
CA 2440760	AA	20020919	CA 2002-2440760	20020313
EP 1368355	A2	20031210	EP 2002-729998	20020313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002008244	A	20040302	BR 2002-8244	20020313
CN 1507447	A	20040623	CN 2002-809688	20020313
JP 2004527508	T2	20040909	JP 2002-571501	20020313
NZ 528639	A	20050729	NZ 2002-528639	20020313
NO 2003004031	A	20031021	NO 2003-4031	20030911
US 2004127508	A1	20040701	US 2003-660794	20030912
ZA 2003007963	A	20040726	ZA 2003-7963	20031013
PRIORITY APPLN. INFO.:			DE 2001-10112197 A	20010314
			DE 2001-10153344 A	20011029
			WO 2002-EP2722 W	20020313

OTHER SOURCE(S): CASREACT 137:232666

GI



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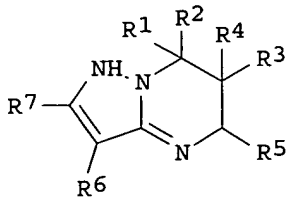
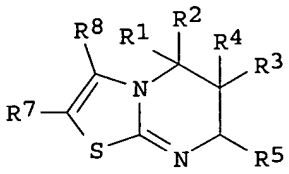
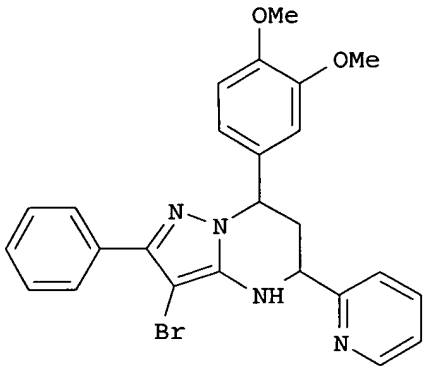


II



III



IV

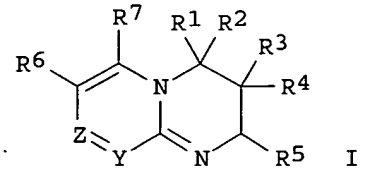
AB Title compds. I, II and III [R1-R4 = H, alkyl, cycloalkyl, etc.; R5 = alkyl, cycloalkyl, aryl, etc.; R6, R7 = H, alkyl, CN, etc.; R8 = H, alkyl, aryl] and their pharmaceutically salts were prepared For example, to a mixture of 5-amino-4-bromo-3-phenylpyrazol (1.5 g) in acetonitrile was added 4-ethenyl-1,2-dimethoxybenzene (1.55 g) 2-pyridinecarboxaldehyde (0.88 g) and trifluoroacetic acid (0.72 mL). The solution was stirred at room temperature until the reaction was completed and then purified by reverse-phase HPLC to provide claimed pyrazolopyrimidine IV. In nucleoside transport protein inhibition studies, 6-examples of compds. I-III exhibited Ki values of 1.3-0.3 μM. Also in NMDA receptor studies, 5-examples of compds. I-III at 10 μM displaced the 3H-(+)MK801 ligand in 75-45%. Compds. I-III are claimed for the treatment of pain, epilepsy, schizophrenia, etc.

L23 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293656 HCAPLUS
DOCUMENT NUMBER: 136:325565
TITLE: Preparation of 3,4-dihydropyrimido[1,2-a]pyrimidines and 3,4-dihydropyrazino[1,2-a]pyrimidines as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna; Jagusch, Utz-Peter
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030934	A1	20020418	WO 2001-EP11702	20011010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10050661	A1	20020418	DE 2000-10050661	20001013
AU 2002014007	A5	20020422	AU 2002-14007	20011010
CA 2425685	AA	20030411	CA 2001-2425685	20011010
EP 1325010	A1	20030709	EP 2001-982417	20011010
EP 1325010	B1	20050427		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014735	A	20031014	BR 2001-14735	20011010
JP 2004511485	T2	20040415	JP 2002-534320	20011010
NZ 525651	A	20041029	NZ 2001-525651	20011010
AT 294180	E	20050515	AT 2001-982417	20011010
NO 2003001588	A	20030408	NO 2003-1588	20030408
US 2003220322	A1	20031127	US 2003-409614	20030409
ZA 2003003634	A	20040812	ZA 2003-3634	20030512

PRIORITY APPLN. INFO.: DE 2000-10050661 A 20001013
WO 2001-EP11702 W 20011010

OTHER SOURCE(S): MARPAT 136:325565
GI



I

AB Title compds. [I; Y = CR8; Z = N; or Y = N; Z = CR9; R1, R2 = H, (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (unsatd.) (substituted) heterocyclyl, (substituted)

(hetero)aryl, (substituted) alkylaryl, etc.; R3, R4 = H, H, (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R5 = (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (unsatd.) (substituted) heterocyclyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R6-R9 = H, F, Cl, Br, iodo, cyano, amino, aminoalkyl, aminodialkyl, etc.] and salts thereof were prepared Several I showed μ-opiate receptor binding with Ki = 1.4-2.5 μM and inhibited at 10 μM NMDA/MK801 binding position with 40-47%. The invention relates also to a method for the production of the title compds., substance libraries containing said compds., medicaments which contain said compds., the use of said compds. in the production of medicaments for treating pain, urinary incontinence, pruritus, tinnitus aurium and/or diarrhea and pharmaceutical prepns. containing said compds.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

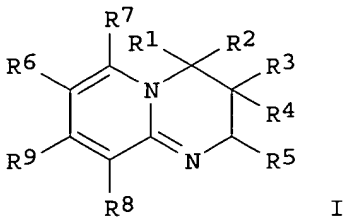
L23 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293655 HCAPLUS
DOCUMENT NUMBER: 136:309934
TITLE: Preparation of 3,4-dihydropyrido[1,2-a]pyrimidines as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna; Jagusch, Utz-Peter
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030933	A1	20020418	WO 2001-EP11700	20011010
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10050662	A1	20020418	DE 2000-10050662	20001013
AU 2002010526	A5	20020422	AU 2002-10526	20011010
CA 2425666	AA	20030411	CA 2001-2425666	20011010
BR 2001014734	A	20030701	BR 2001-14734	20011010
EP 1326866	A1	20030716	EP 2001-978402	20011010
EP 1326866	B1	20050615		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004511484	T2	20040415	JP 2002-534319	20011010
NZ 525652	A	20050128	NZ 2001-525652	20011010
AT 297927	E	20050715	AT 2001-978402	20011010
NO 2003001412	A	20030422	NO 2003-1412	20030327
US 2003229104	A1	20031211	US 2003-411390	20030411
ZA 2003003640	A	20040812	ZA 2003-3640	20030512

PRIORITY APPLN. INFO.:

DE 2000-10050662	A	20001013
WO 2001-EP11700	W	20011010

OTHER SOURCE(S): MARPAT 136:309934
GI



I

AB Title compds. [I; R1, R2 = H, OR10, SH, SR10, (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (unsatd.), (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R3, R4 = H, H, (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R5 = (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.; R6-R9 = H, F, Cl, Br, I, cyano, amino, aminoalkyl, aminodialkyl, etc.; R10 = (branched) (unsatd.) (substituted) alkyl, (unsatd.) (substituted) cycloalkyl, (substituted) (hetero)aryl, (substituted) alkylaryl, etc.] and salts thereof were prepared as analgesics (no data). The invention relates also to a method for the production of the title compds., substance libraries containing said compds., medicaments which contain said compds., the use of said compds. in the production of medicaments for treating pain, urinary incontinence, pruritus, tinnitus aurium and/or diarrhea and pharmaceutical prepns. containing said compds.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:293606 HCAPLUS
DOCUMENT NUMBER: 136:325421
TITLE: Preparation of (hetero)arylsulfonylguanidines for treatment of pain, epilepsy, migraine, etc.
INVENTOR(S): **Gerlach, Matthias**; Uragg, Heinz; Haurand, Michael; Puetz, Claudia Katharina; Maul, Corinna; Chizh, Boris
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030881	A1	20020418	WO 2001-EP11245	20011001

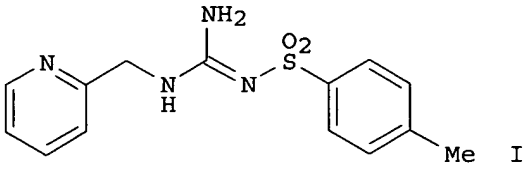
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10048716	A1	20020418	DE 2000-10048716		20000930
DE 10112068	A1	20020926	DE 2001-10112068		20010312
AU 2001093852	A5	20020422	AU 2001-93852		20011001
CA 2424107	AA	20030328	CA 2001-2424107		20011001
EP 1320520	A1	20030625	EP 2001-974309		20011001
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004511463	T2	20040415	JP 2002-534269		20011001
US 2003225084	A1	20031204	US 2003-402382		20030331
PRIORITY APPLN. INFO.:			DE 2000-10048716	A	20000930
			DE 2001-10112068	A	20010312
			WO 2001-EP11245	W	20011001

OTHER SOURCE(S): MARPAT 136:325421

GI



I

AB R1SO2N:C(NH2)NR2R3, R1SO2NHC(:NH)NR2R3 [R1 = (unsatd.) (substituted) alkyl, cycloalkyl, aryl, heteroaryl; R2 = (unsatd.) (substituted) alkyl, cycloalkyl, aryl, heteroaryl, arylamino, arylsulfonyl, aralkyl, amino, etc.; R3 = H, (unsatd.) (substituted) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, cycloalkylalkyl, heteroarylalkyl; R2R3 = (CH2)3-4, CH2CH2OCH2CH2, CH2CH2NR8CH2CH2; R8 = (unsatd.) (substituted) alkyl, cycloalkyl, aryl, heteroaryl, aralkyl, cycloalkylalkyl, heteroarylalkyl], were prepared Using a robotic synthesis apparatus, N-[(3,5-dimethylpyrazol-1-yl)iminomethyl]-4-methylbenzenesulfonamide, MeSO3H, and 2-picolylamine were stirred 45 h in MeCN at 110° to give title compound (I). I showed analgesic activity in the Chung rat test with ED50 = 10-20 mg/kg.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:220547 HCAPLUS

DOCUMENT NUMBER: 136:247352

TITLE: Method for producing chiral formylamino(alkylthio)alkanoates

INVENTOR(S): **Gerlach, Matthias**; Puetz, Claudia; Enders, D.; Gaube, Gero

PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany

SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022569	A1	20020321	WO 2001-EP10626	20010914
WO 2002022569	C1	20020613		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10045832	A1	20020529	DE 2000-10045832	20000914
AU 2002012241	A5	20020326	AU 2002-12241	20010914
CA 2422024	AA	20030312	CA 2001-2422024	20010914
EP 1317427	A1	20030611	EP 2001-980386	20010914
EP 1317427	B1	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509102	T2	20040325	JP 2002-526822	20010914
BR 2001013944	A	20040622	BR 2001-13944	20010914
AT 284867	E	20050115	AT 2001-980386	20010914
ES 2234908	T3	20050701	ES 2001-1980386	20010914
NO 2003001137	A	20030505	NO 2003-1137	20030312
US 2003236429	A1	20031225	US 2003-387870	20030314
ZA 2003002824	A	20040511	ZA 2003-2824	20030410
HK 1052923	A1	20050630	HK 2003-105139	20030716
PRIORITY APPLN. INFO.:			DE 2000-10045832 A	20000914
			WO 2001-EP10626 W	20010914

OTHER SOURCE(S): CASREACT 136:247352; MARPAT 136:247352

AB R2CH2CR1(SR4)CH(NHCHO)CO2R3 [R1-R3 = (un)substituted aliphatic; R4 = (un)substituted alkyl, cycloalkyl, aryl, heteroaryl] are prepared by Michael reaction of R2CH2CR1:C(NHCHO)CO2R3 with R4SH as its Li enolate in presence of a chiral ligand, such as (S,S)-MeOCHPhCHPhOMe, a Lewis acid or Bronsted base, followed by base hydrolysis. Thus, glycine was esterified, N-formylated, and dehydrated to CNCH2CO2Et which was treated with 2-heptanone to give (E,Z)-Me(CH2)4CHMe:C(CO2Et)NHCHO (I). PhCH2SH was treated with BuLi in THF, followed by (E)-I or (Z)-I, followed by hydrolysis with NaOH to give Me(CH2)4CMe(SCH2Ph)CH(NHCHO)CO2Et whose diastereomers were obtained in high de by separation by HPLC or crystallization from pentane-EtOH. The use of the chiral ligand did not significantly alter the diastereomeric ratio.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:220546 HCAPLUS
DOCUMENT NUMBER: 136:247888
TITLE: Preparation of β-thio-α-amino acids for use as medicaments for the treatment of pain or disease
INVENTOR(S): Chizh, Boris; **Gerlach, Matthias**; Haurand, Michael; Putz, Claudia; Gaube, Gero; Enders, D.
PATENT ASSIGNEE(S): Grunenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002022568	A1	20020321	WO 2001-EP10488		20010911
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
DE 10045831	A1	20020404	DE 2000-10045831		20000914
DE 10049484	A1	20020502	DE 2000-10049484		20000929
AU 2002014978	A5	20020326	AU 2002-14978		20010911
CA 2421990	AA	20030312	CA 2001-2421990		20010911
EP 1317426	A1	20030611	EP 2001-983480		20010911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004509101	T2	20040325	JP 2002-526821		20010911
US 2003236253	A1	20031225	US 2003-387843		20030314
US 6846843	B2	20050125			
PRIORITY APPLN. INFO.:			DE 2000-10045831	A	20000914
			DE 2000-10049484	A	20000929
			WO 2001-EP10488	W	20010911

OTHER SOURCE(S): MARPAT 136:247888

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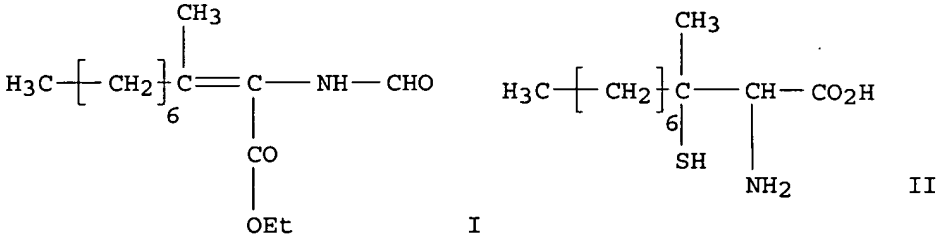

I II

AB Title compds. R(R1)(SR2)CCH(NH2)CO2H [R, R1 independently = H, (un)branched (un)substituted (un)saturated alkyl, CH2Ph, aryl, cycloalkyl, heteroaryl; R,R1 together = (un)saturated (un)substituted (heterocyclic) ring; R2 = H, (un)branched (un)substituted (un)saturated alkyl, (un)substituted (un)saturated cycloalkyl; (un)substituted (hetero)aryl] in the form of racemates, enantiomers, or diastereomers and their physiol. acceptable salts were prepared and tested as gabapentin analogs for use in the treatment of pain and other conditions. Thus, glycine was transformed into its Et ester hydrochloride, which was N-formylated and reduced to its isocyanate. The isocyanate was then condensed with 2-nonanone using potassium tert-butylate to give (I) as a E/Z mixture, which was then reacted with P4S10, giving the protected mercapto compound, which was deprotected to give (II) as a racemic mixture of the erythro and threo isomers. In in vitro binding affinity tests with gabapentin, II had IC50 of 199 nM. In in vivo writhing mouse tests, II had ED50 of 35 mg/kg (i.v.); in mouse formalin tests, II had ED50 of 66 mg/kg (i.v.); in a paw incision test in rats, II had maximum possible effect (MPE) of 27%, at 464 mg/kg i.p., compared to 66% MPE at 100 mg/kg.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:798222 HCAPLUS
DOCUMENT NUMBER: 135:344484
TITLE: Preparation of N-acylimidazopyridineamine chlorides and analogs as μ-opiate receptor ligands
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001081344	A1	20011101	WO 2001-EP3772		20010403
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
DE 10019714	A1	20020110	DE 2000-10019714		20000420
CA 2402808	AA	20011101	CA 2001-2402808		20010403
EP 1274709	A1	20030115	EP 2001-931560		20010403
EP 1274709	B1	20040922			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003531208	T2	20031021	JP 2001-578434		20010403
BR 2001010357	A	20040420	BR 2001-10357		20010403
NZ 521069	A	20040730	NZ 2001-521069		20010403
AT 277045	E	20041015	AT 2001-931560		20010403
ES 2227186	T3	20050401	ES 2001-1931560		20010403
NO 2002004838	A	20021007	NO 2002-4838		20021007
US 2003119842	A1	20030626	US 2002-273344		20021018
ZA 2002009408	A	20040219	ZA 2002-9408		20021119
HK 1052703	A1	20050422	HK 2003-105003		20030710
PRIORITY APPLN. INFO.:			DE 2000-10019714	A	20000420
			WO 2001-EP3772	W	20010403

OTHER SOURCE(S): MARPAT 135:344484
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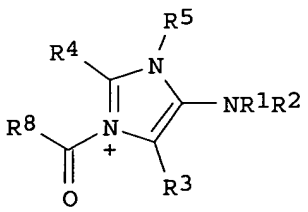

I

AB Title compds. (ICl-)[II; R1 = CMe3, cyclohexyl, CH2CO2Me, (un)substituted Ph, etc.; R2 = H or alkanoyl; R3 = Me, Ph, 2-furyl, 2-pyridinyl, etc.;

R4R5 = (un)substituted CH:CHCH:CH, CH:NCH:CH, N:CHCH:CH, etc.; R8 = (cyclo)alkyl] were prepared Thus, 2-aminopyridine was cyclocondensed with Me3CNC and PhCHO to give, after N-acylation, II (R1 = CMe3, R2 = H, R3 = Ph, R4R5 = CH:CHCH:CH, R8 = Me). Data for biol. activity of II were given.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:597963 HCAPLUS
DOCUMENT NUMBER: 135:180709
TITLE: Substituted 1,2,3,4-tetrahydroquinoline-2-carboxylic acid derivatives
INVENTOR(S): **Gerlach, Matthias**; Przewosny, Michael; Englberger, Werner; Reissmueller, Elke; Bloms-Funke, Petra; Maul, Corinna; Jagusch, Utz-Peter
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058875	A2	20010816	WO 2001-EP588	20010119
WO 2001058875	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10005302	A1	20020117	DE 2000-10005302	20000207
CA 2416343	AA	20010816	CA 2001-2416343	20010119
EP 1254118	A2	20021106	EP 2001-901176	20010119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003522758	T2	20030729	JP 2001-558426	20010119
NZ 521088	A	20040528	NZ 2001-521088	20010119
US 2003087926	A1	20030508	US 2002-213436	20020807
US 6699877	B2	20040302		
PRIORITY APPLN. INFO.:			DE 2000-10005302 A	20000207
			WO 2001-EP588 W	20010119

OTHER SOURCE(S): MARPAT 135:180709
AB The invention concerns substituted 1,2,3,4-tetrahydroquinoline-2-carboxylic acid derivs., a method for the production of these derivs., their use in the production of medicaments and medicaments containing these compds. for use as analgesics.

L23 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:489366 HCAPLUS
DOCUMENT NUMBER: 135:92541
TITLE: Preparation of a substance library from iminium salts and naphthalene, pyrrole, and/or indole compounds and

use of the library in discovery of active compounds.
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047882	A2	20010705	WO 2000-EP12973	20001220
WO 2001047882	A3	20020530		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19963177	A1	20010712	DE 1999-19963177	19991227

PRIORITY APPLN. INFO.: DE 1999-19963177 A 19991227
OTHER SOURCE(S): MARPAT 135:92541
AB A substance library was prepared by (1) reaction of aldehydes with secondary amines in the presence of base to give aminals, (2) treatment of the aminals with acid chlorides to give iminium salts, (3) reaction of the iminium salts with naphthalene, pyrrole, or indole compds. Thus, reaction of 1H-indole with benzylidenedimethylammonium chloride gave [(1H-indol-3-yl)phenylmethyl]dimethylamine. The latter gave 41% inhibition of phenylquinone-induced writhing in mice.

L23 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:489363 HCAPLUS
DOCUMENT NUMBER: 135:76789
TITLE: Preparation of 2-[amino(aryl)methyl]pyrroles as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047878	A1	20010705	WO 2000-EP12976	20001220

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19963174	A1	20010712	DE 1999-19963174	19991227
CA 2396502	AA	20010705	CA 2000-2396502	20001220
BR 2000016814	A	20020910	BR 2000-16814	20001220
EP 1246799	A1	20021009	EP 2000-991220	20001220
EP 1246799	B1	20031015		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003527350	T2	20030916	JP 2001-549351	20001220
AT 252077	E	20031115	AT 2000-991220	20001220
NZ 519975	A	20040227	NZ 2000-519975	20001220
PT 1246799	T	20040331	PT 2000-991220	20001220
ES 2208466	T3	20040616	ES 2000-991220	20001220
ZA 2002004199	A	20040210	ZA 2002-4199	20020527
NO 2002003028	A	20020820	NO 2002-3028	20020621
US 2003023100	A1	20030130	US 2002-168964	20020625
HK 1051855	A1	20040723	HK 2003-102525	20030409
PRIORITY APPLN. INFO.:			DE 1999-19963174 A	19991227
			WO 2000-EP12976 W	20001220

OTHER SOURCE(S): MARPAT 135:76789
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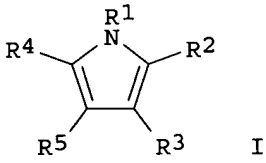

I

AB Title compds. [I; R1 = H, alkyl, aryl, heteroaryl, etc.; R2 = CHR6NR7R8; R3-R5 = H, F, Cl, Br, CF3, cyano, NO2, etc.; R6 = (substituted) Ph; R7, R8 = (substituted) alkyl, Ph, PhCH2, PhEt; R7R8 = (CH2)2O(CH2)2, (CH2)n; n = 3-6] were prepared Thus, 4-(2-methoxybenzylidene)morpholin-4-ium chloride (preparation given) was stirred with 1-phenyl-1H-pyrrole at 18° for 16 h in a Zymark device to give 4-[(2-methoxyphenyl)-(1-phenyl-1H-pyrrol-2-yl)methyl]morpholine. Several I inhibited serotonin reuptake by 39-83% and inhibited phenylquinone-induced writhing in mice by 17-87%.
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:489352 HCAPLUS
DOCUMENT NUMBER: 135:76698
TITLE: Preparation of α-aminobenzylnaphthols and analogs as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047866	A1	20010705	WO 2000-EP12972	20001220
WO 2001047866	C2	20021107		

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        W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
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            IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
            MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
            SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
            DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
            BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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    CA 2394098           AA    20010705    CA 2000-2394098         20001220
    BR 2000016781        A     20020827    BR 2000-16781           20001220
    EP 1246790           A1    20021009    EP 2000-990799          20001220
    EP 1246790           B1    20050504
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            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
    JP 2003519115        T2    20030617    JP 2001-549340          20001220
    NZ 519976            A     20040430    NZ 2000-519976          20001220
    AU 775709            B2    20040812    AU 2001-30147           20001220
    AT 294773            E     20050515    AT 2000-990799          20001220
    ZA 2002004289        A     20040210    ZA 2002-4289            20020529
    NO 2002002896        A     20020617    NO 2002-2896            20020617
    US 2004044061        A1    20040304    US 2002-149449          20020627
    US 6774136           B2    20040810
    US 2004147570        A1    20040729    US 2004-757581          20040115
PRIORITY APPLN. INFO.:                       DE 1999-19963179    A   19991227
                                             WO 2000-EP12972     W   20001220
                                             US 2002-149449      A3  20020627
OTHER SOURCE(S):         MARPAT 135:76698
GI
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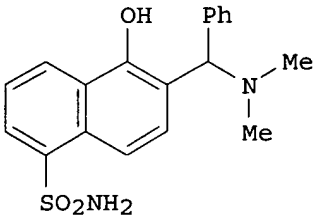

II

AB R12OZCHR9NR10R11 [I; R9 = alkyl, (hetero)aryl, etc.; R10,R11 = (un)substituted alk(en)yl, -Ph, -CH2Ph, etc.; R12 = (un)substituted 1,2- or 2,1-naphthylene] were prepared Thus, PhCHO was condensed with Me2NH and the product used to alkylate 5-hydroxy-1-naphthalenesulfonamide to give title compound II. Data for biol. activity of I were given.

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REFERENCE COUNT:         3     THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23  ANSWER 22 OF 30  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2001:488531  HCAPLUS
DOCUMENT NUMBER:         135:92540
TITLE:                   Preparation of 3-[amino(aryl)methyl]indoles as
                         analgesics
INVENTOR(S):             Maul, Corinna; Gerlach, Matthias
PATENT ASSIGNEE(S):      Gruenenthal G.m.b.H., Germany
SOURCE:                  Ger. Offen., 40 pp.
                         CODEN: GWXXBX
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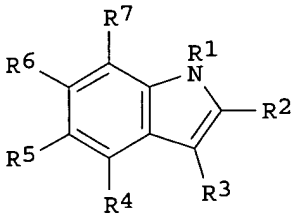
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19963178	A1	20010705	DE 1999-19963178	19991227
CA 2392866	AA	20010705	CA 2000-2392866	20001220
WO 2001047885	A1	20010705	WO 2000-EP12974	20001220
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000016747	A	20020903	BR 2000-16747	20001220
EP 1261585	A1	20021204	EP 2000-991219	20001220
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003519124	T2	20030617	JP 2001-549357	20001220
NZ 518876	A	20050225	NZ 2000-518876	20001220
ZA 2002003444	A	20030430	ZA 2002-3444	20020430
NO 2002002803	A	20020612	NO 2002-2803	20020612
US 2003060497	A1	20030327	US 2002-168985	20020626
PRIORITY APPLN. INFO.:			DE 1999-19963178 A	19991227
			WO 2000-EP12974 W	20001220

OTHER SOURCE(S): MARPAT 135:92540
GI



I

AB Title compds. [I; R1 = H, alkyl, aralkyl, heteroarylalkyl; R2, R4-R7 = H, F, Cl, Br, CF3, cyano, NO2, NHR8, SR9, OR10, SO2NH2, SO2NHR21, CO2R11, CH2CO2R12, COR19, alkyl, aryl, heteroaryl, aralkyl, heteroarylalkyl; R3 = CHR13NR14R15, etc.; R8 = H, COR16, alkyl, aryl, etc.; R9, R11, R12 = H, alkyl, aryl, etc.; R10 = H, COR17, alkyl, (alkenyl) aryl, heteroaryl, etc.; R13 = aryl, heteroaryl, alkyl, etc.; R14, R15 = alkyl, aryl, alkenylaryl, etc.; R16 = alkyl, aryl, heteroaryl, etc.; R17 = alkyl, etc.; R18 = alkyl, aryl, heteroaryl, naphthyl, etc.; R19 = H, NHNH2, NHR20, alkyl, aryl, heteroaryl, etc.; R20 = H, alkyl, aryl, (alkenyl) aryl, heteroaryl, etc.; R21 = H, COR17, alkyl, aryl, etc.] were prepared Thus, benzylidenedimethylammonium chloride (preparation given) was stirred with Et 1H-indolecarboxylate at 15° for 11 h in a Zymark device to give Et 3-(dimethylaminophenylmethyl)-1H-indole-2-carboxylate. I at 10 mg/kg i.v. gave 6-82% inhibition of phenylquinone-induced writhing in mice.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283961 HCAPLUS
DOCUMENT NUMBER: 134:295826
TITLE: Preparation of imidazopyridineamines and analogs as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027119	A2	20010419	WO 2000-EP9098	20000918
WO 2001027119	A3	20011011		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19948434	A1	20010607	DE 1999-19948434	19991008
PT 1218378	T	20030930	PT 2000-969439	20001006
ES 2198355	T3	20040201	ES 2000-969439	20001006
ZA 2002003579	A	20030806	ZA 2002-3579	20020506
ZA 2002003581	A	20031126	ZA 2002-3581	20020506

PRIORITY APPLN. INFO.: DE 1999-19948434 A 19991008
OTHER SOURCE(S): MARPAT 134:295826
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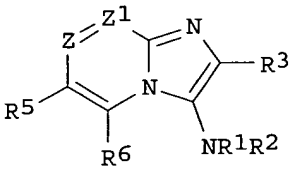

I

AB Substance libraries comprising, e.g., I [R1 = CMe3, cycloalkyl, (un)substituted Ph, etc.; R2 = H, cycloalkyl, alkanoyl, etc.; R3 = (cyclo)alkyl, (un)substituted (hetero)aryl, etc.; R5,R6 = H, halo, alkyl, alkoxy, etc.; Z = N or CR10; Z1 = N or CR9; R9,R10 = groups cited for R5; Z = N ≠ Z1; Z1 = N ≠ Z] were prepared Thus, pyridine-2-amine was cyclocondensed with cyclohexanecarboxaldehyde and tert-Bu isocyanide to give I (R1 = CMe3, R2 = R5 = R6 = H, R3 = cyclohexyl, Z = Z1 = CH). Data for biol. activity of I were given.

L23 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283960 HCAPLUS
DOCUMENT NUMBER: 134:295829

TITLE: Preparation of aminoimidazo[2,1-b]thiazoles, -pyrazoles, and -triazoles as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027118	A2	20010419	WO 2000-EP9097	20000918
WO 2001027118	A3	20010920		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19948434	A1	20010607	DE 1999-19948434	19991008
DE 19948436	A1	20010607	DE 1999-19948436	19991008
CA 2388476	AA	20010419	CA 2000-2388476	20000918
BR 2000014817	A	20020618	BR 2000-14817	20000918
EP 1218383	A2	20020703	EP 2000-967693	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003511456	T2	20030325	JP 2001-530336	20000918
NZ 518390	A	20031031	NZ 2000-518390	20000918
AU 781227	B2	20050512	AU 2000-77772	20000918
NO 2002001566	A	20020527	NO 2002-1566	20020403
US 2002183320	A1	20021205	US 2002-117335	20020408
US 6657064	B2	20031202		
ZA 2002003582	A	20030905	ZA 2002-3582	20020506
US 2004023927	A1	20040205	US 2003-633579	20030805
US 6936631	B2	20050830		

PRIORITY APPLN. INFO.:

DE 1999-19948434	A	19991008
DE 1999-19948436	A	19991008
DE 1999-19948438	A	19991008
WO 2000-EP9097	W	20000918
US 2002-117335	A3	20020408

OTHER SOURCE(S): MARPAT 134:295829
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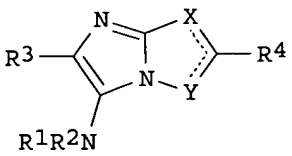

I

AB Title compds. [I; R1 = CMe3, cyanohexyl, (substituted) Ph, cycloalkyl, etc.; R2 = H, (branched) (substituted) alkylcarbonyl, Ph, naphthyl, pyridyl, thiazolyl, furoyl, etc.; R3 = (branched) alkylcycloalkyl,

(substituted) Ph, naphthyl, quinolinyl, anthracenyl, phenanthrenyl, etc.; X = CR5, N, S; Y = N, but when X = S, Y = CR6, N; R4, R5, R6 = H, (branched) alkyl, halo, CF3, cyano, NO2, amino, etc.], were prepared Using a Zymark robotic synthesis system, 3-amino-1,2,4-triazole and HClO4 in CH2Cl2, furfural in CH2Cl2, and tert-butylisonitrile in CH2Cl2 were added successively to a reactor tube at 15° followed by 11 h stirring at 15° to give tert-butyl-(5-furan-2-yl-imidazo[1,2-b][1,2,4]triazol-6-yl)amine. Several I at 10 μM showed 34-77% α2 adrenoceptor affinity.

L23 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283953 HCAPLUS
DOCUMENT NUMBER: 134:295841
TITLE: Preparation of aminoimidazo[1,2-a]pyridines, -pyrimidines, and -pyrazines as analgesics.
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027111	A2	20010419	WO 2000-EP9096	20000918
WO 2001027111	A3	20010614		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19948434	A1	20010607	DE 1999-19948434	19991008
DE 19948438	A1	20010607	DE 1999-19948438	19991008
DE 19948438	B4	20040415		
CA 2382919	AA	20010419	CA 2000-2382919	20000918
BR 2000014818	A	20020618	BR 2000-14818	20000918
EP 1218382	A2	20020703	EP 2000-967692	20000918
EP 1218382	B1	20040128		
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JP 2003511451	T2	20030325	JP 2001-530329	20000918
NZ 518439	A	20031031	NZ 2000-518439	20000918
AT 258554	E	20040215	AT 2000-967692	20000918
PT 1218382	T	20040630	PT 2000-967692	20000918
ES 2213611	T3	20040901	ES 2000-967692	20000918
AU 779197	B2	20050113	AU 2000-77771	20000918
NO 2002001565	A	20020527	NO 2002-1565	20020403
US 2003018032	A1	20030123	US 2002-117333	20020408
US 6638933	B2	20031028		
HK 1047747	A1	20041203	HK 2002-109382	20021228

PRIORITY APPLN. INFO.:
DE 1999-19948434 A 19991008
DE 1999-19948438 A 19991008
WO 2000-EP9096 W 20000918

OTHER SOURCE(S): MARPAT 134:295841

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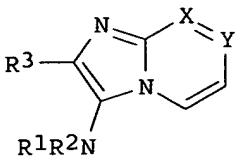

I

AB Title compds. [I; X, Y = CH, N; X and Y cannot simultaneously = N; R1 = tert-Bu, cyanoalkyl, (substituted) Ph, cycloalkyl, etc.; R2 = H, (substituted) alkylcarbonyl, Ph, naphthyl, pyridyl, etc.; R3 = alkyl, cycloalkyl, Ph, PhO, (substituted) naphthyl, pyrrolyl, pyridyl, etc.] were prepared Using a Zymark robotic synthesis system, 2-aminopyridine and HClO4 in CH2Cl2, pyridine-2-carboxaldehyde in CH2Cl2, and 1,6-diisocyanohexane in CH2Cl2 were added successively to a reaction tube at 15° followed by 11 h stirring at 15° to give (6-isocyanohexyl)-(2-pyridin-2-ylimidazo[1,2-a]pyridin-3-yl)amine. Tested I at 10 mg/kg i.v. in mice gave 53-90% inhibition of phenylquinone-induced writhing.

L23 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283952 HCAPLUS
DOCUMENT NUMBER: 134:311219
TITLE: Preparation of aminoimidazo[1,2-a]pyridines, -quinolines, and -pyrimidines as analgesics
INVENTOR(S): **Gerlach, Matthias**; Maul, Corinna
PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027110	A2	20010419	WO 2000-EP9095	20000918
WO 2001027110	A3	20010920		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19948434	A1	20010607	DE 1999-19948434	19991008
DE 19948437	A1	20010607	DE 1999-19948437	19991008
CA 2386813	AA	20010419	CA 2000-2386813	20000918
EP 1218380	A2	20020703	EP 2000-964191	20000918
EP 1218380	B1	20031217		
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BR 2000014826	A	20020827	BR 2000-14826	20000918
JP 2003517466	T2	20030527	JP 2001-530328	20000918
AT 256684	E	20040115	AT 2000-964191	20000918

PT 1218380	T	20040531	PT 2000-964191		20000918
ES 2213044	T3	20040816	ES 2000-964191		20000918
NZ 518637	A	20041224	NZ 2000-518637		20000918
AU 780823	B2	20050421	AU 2000-75199		20000918
NO 2002001563	A	20020604	NO 2002-1563		20020403
US 2002183327	A1	20021205	US 2002-117334		20020408
US 6849642	B2	20050201			
ZA 2002003580	A	20030806	ZA 2002-3580		20020506
HK 1047748	A1	20041021	HK 2002-109383		20021228
PRIORITY APPLN. INFO.:			DE 1999-19948434	A	19991008
			DE 1999-19948437	A	19991008
			WO 2000-EP9095	W	20000918

OTHER SOURCE(S): MARPAT 134:311219

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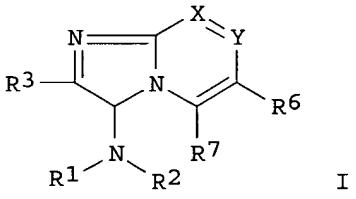


I

AB The title compds. [I; X, Y = CR4, N; X and Y cannot simultaneously = N; R4, R6, R7 = H, (branched) alkyl, NO2, amino, OH, CF3, halo, etc.; R1 = cyanoalkyl, (substituted) Ph, cycloalkyl, etc.; R2 = H, (branched) (substituted) alkylcarbonyl, Ph, naphthyl, pyridyl, thiazolyl, etc.; R3 = (branched) alkyl, cycloalkyl, (substituted) Ph, naphthyl, pyrrolyl, pyridyl, etc.] were prepared Using a Zymark robotic synthesis system, 2,6-diamino-4-chloropyrimidine and HClO4 in CH2Cl2, furfural in CH2Cl2, and 1,6-diisocyanohexane in CH2Cl2 were added successively to a reaction tube at 15° followed by 11 h stirring at 15° to give 7-chloro-2-furan-2-yl-(6-isocyanohexyl)-imidazo[1,2-a]pyrimidin-3,5-diamine. Several I at 10 μM showed 51-100% α2 adrenoceptor affinity.

L23 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:283951 HCAPLUS
DOCUMENT NUMBER: 134:305332
TITLE: Tert-butyl-(7-methyl-imidazo[1,2-a]pyridine-3-yl)amine derivatives, preparation method, pharmaceutical compositions, and therapeutic use
INVENTOR(S): Maul, Corinna; Sundermann, Bernd; Hennies, Hagen-Heinrich; Schneider, Johannes; **Gerlach, Matthias**
PATENT ASSIGNEE(S): Grunenthal G.m.b.H., Germany
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027109	A2	20010419	WO 2000-EP9791	20001006
WO 2001027109	A3	20010920		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

DE 19948434	A1	20010607	DE 1999-19948434		19991008
CA 2386804	AA	20010419	CA 2000-2386804		20001006
EP 1218378	A2	20020703	EP 2000-969439		20001006
EP 1218378	B1	20030423			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003511450	T2	20030325	JP 2001-530327		20001006
AT 238304	E	20030515	AT 2000-969439		20001006
BR 2000014827	A	20030708	BR 2000-14827		20001006
PT 1218378	T	20030930	PT 2000-969439		20001006
ES 2198355	T3	20040201	ES 2000-969439		20001006
NZ 518438	A	20040827	NZ 2000-518438		20001006
AU 780526	B2	20050324	AU 2000-79153		20001006
NO 2002001564	A	20020604	NO 2002-1564		20020403
US 2003022914	A1	20030130	US 2002-117339		20020408
US 6703404	B2	20040309			
ZA 2002003579	A	20030806	ZA 2002-3579		20020506
ZA 2002003581	A	20031126	ZA 2002-3581		20020506
HK 1047749	A1	20030822	HK 2002-109385		20021228
PRIORITY APPLN. INFO.:			DE 1999-19948434	A	19991008
			WO 2000-EP9791	W	20001006

OTHER SOURCE(S): MARPAT 134:305332

AB The invention provides tert-butyl-(7-methyl-imidazo[1,2-a]pyridine-3-yl)amine derivs., as well as a method for their preparation and medicaments containing them. The invention further provides the use of these compds. in the production of a medicament for the inhibition of the NO synthase and for the treatment of e.g. migraine, as well as pharmaceutical compns. containing them.

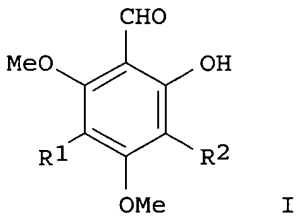
L23 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:281298 HCAPLUS
DOCUMENT NUMBER: 131:130139
TITLE: Metalated 2-alkenyl sulfoximines in asymmetric synthesis. Regio- and stereoselective synthesis of highly substituted oxabicyclic ethers and studies towards the total syntheses of the euglobals G1 and G2 and arenaran A
AUTHOR(S): Reggelin, Michael; **Gerlach, Matthias**; Vogt, Melanie
CORPORATE SOURCE: Institut Organische Chemie, Johann Wolfgang Goethe Univ., Frankfurt/Main, D-60439, Germany
SOURCE: European Journal of Organic Chemistry (1999), (5), 1011-1031
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:130139

AB 2-Cyclopentenyl- and 2-cyclohexenylmethyl sulfoximines are converted into angular C-functionalized, highly substituted, isomerically pure (ds ≥ 98%) 2-oxabicyclo[3.3.0]octanes and 2-oxabicyclo[3.4.0]nonanes in

high yields by a convenient 1-pot sequence. In addition to the methodol. work, studies towards the total synthesis of the euglobals G1 and G2 and arenaran A are reported.

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:304772 HCAPLUS
DOCUMENT NUMBER: 127:50341
TITLE: Application of the 1,n-ADEQUATE experiment in the assignment of highly substituted aromatic compounds
AUTHOR(S): Kock, Matthias; Reif, Bernd; **Gerlach, Matthias**; Reggelin, Michael
CORPORATE SOURCE: Institut fur Organische Chemie, Johann Wolfgang Goethe-Universitat, Frankfurt/Main, D-60439, Germany
SOURCE: Molecules [Electronic Publication] (1996), 1, 41-45
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://science.springer/de/molec/bibs/1996/601004 1.html
PUBLISHER: Molecular Diversity Preservation International
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
GI



I

AB This communication describes the 1,n-ADEQUATE experiment to differentiate between two possible products I (R1 = H, Me2CHCH2CO; R2 = Me2CHCH2CO, H) from acylation of 2-Hydroxy-4,6-dimethoxy-benzaldehyde. The ADEQUATE expts. are new NMR based methods for assigning the constitution of natural products, combining a HSQC or HMBC step with a C,C correlation in natural abundance. The 1,n-ADEQUATE technique allows to observe pseudo 4JCH correlations which were necessary for the distinction of products I. Different NMR methods for the constitutional assignment of natural products and other organic mols. are discussed in detail. This communication also demonstrates that the 1,n-ADEQUATE method is generally applicable for the constitutional assignment of highly substituted aromatic compds. as well as for the localization of O-acetyl groups bound to quaternary carbons.

L23 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:268459 HCAPLUS
DOCUMENT NUMBER: 125:57543
TITLE: Metalated 2-Alkenylsulfoximines: Efficient Solutions for Asymmetric d3-Synthons
AUTHOR(S): Reggelin, Michael; Weinberger, Heinz; **Gerlach, Matthias**; Welcker, Reinhard
CORPORATE SOURCE: Institut fuer Organische Chemie, Johann-Wolfgang-Goethe-Universitaet, Frankfurt/Main, D-60439, Germany
SOURCE: Journal of the American Chemical Society (1996), 118(20), 4765-77

CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:57543
AB By starting from the 4,5-dihydro-1,2λ6,3-oxathiazole 2-oxides or their enantiomers, a number of enantiopure acyclic and cyclic 2-alkenyl sulfoximines have been prepared After deprotonation with n-BuLi and transmetalation with chlorotris(isopropoxy)titanium, these sulfoximines can be γ-hydroxyalkylated to the corresponding γ-hydroxy vinyl sulfoximines with high diastereomeric excesses (≥95% de) irresp. of the nature of the added aldehyde. The cyclopentenyl- and cyclohexenylsulfoximines are demonstrated as the first examples of highly enantioselective solns. for cyclic d3-synthons. From the x-ray structures it can be deduced that the SS/RS-configured sulfoximines attack the aldehydes nearly exclusively from their Re/Si faces, resp. A remarkable property of these systems is that this stereochem. interrelation holds also for reactions with chiral aldehydes (reagent control), although here the achievable stereocontrol depends on the relative configuration of the stereogenic centers in the auxiliary. This is especially true for the cyclohexenylsulfoximines which require the same absolute configuration at both the sulfur atom and the carbon atom in the side chain of the amino acid based auxiliary. In the case of this intramol. matched situation, the stereochem. preferences of the chiral aldehyde can be overcompensated nearly completely. This mutual reinforcement of the two stereogenic centers in the sulfoximine moiety accounts for the high degree of reagent control (≥94% de in the acyclic series, ≥95% de with the five-membered ring systems, and ≥97% de with the cyclohexenylsulfoximines) achievable with these 2-alkenylsulfoximines.

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L5              STR
L7              STR
L11             STR
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L17             STR
L18             STR
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                  PETER"/AU)
L25            38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 NOT (L20 OR L23)


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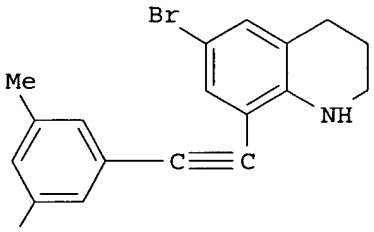
L25  ANSWER 1 OF 38  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:348098  HCAPLUS
DOCUMENT NUMBER:         143:26477
TITLE:                   Palladium(II)-catalyzed heterocyclization of
                         8-arylethynyl-1,2,3,4-tetrahydroquinolines: A facile
                         route to 2-aryl-5,6-dihydro-4H-pyrrolo[3,2,1-
```

ij]quinoline derivatives
AUTHOR(S): Marchand, Pascal; Puget, Alain; Le Baut, Guillaume; **Emig, Peter**; Czech, Michael; Guenther, Eckhard
CORPORATE SOURCE: Laboratoires de Chimie Organique et de Chimie Therapeutique, UPRES EA 1155, Faculte de Pharmacie, Nantes, F-44035, Fr.
SOURCE: Tetrahedron (2005), 61(16), 4035-4041
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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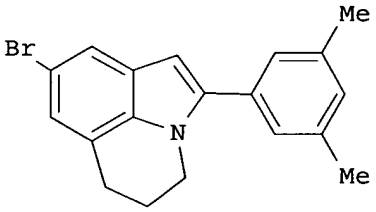


II

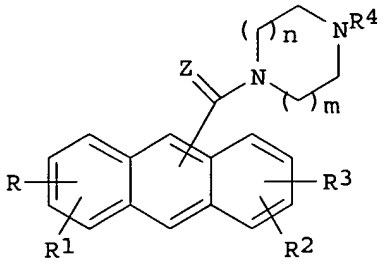
AB Dihydropyrroloquinolines have been synthesized reacting 8-arylethynyl-1,2,3,4-tetrahydroquinolines in the presence of palladium(II) chloride catalyst. Heteroannulation has been achieved in good yields and tolerates substituents on the tetrahydroquinoline, including bromo, cyano, and ester. E.g., PdCl2 catalyzed the heterocyclization of 8-arylethynyl-1,2,3,4-tetrahydroquinoline I to give 2-aryl-5,6-dihydro-4H-pyrrolo[3,2,1-ij]quinoline II.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 2 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:75996 HCAPLUS
DOCUMENT NUMBER: 140:146164
TITLE: Preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Aue, Beate; Polymeropoulos, Emmanuel; Baasner, Silke; Schmidt, Peter
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: Ger. Offen., 31 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10232525	A1	20040129	DE 2002-10232525	20020718
PRIORITY APPLN. INFO.:			DE 2002-10232525	20020718

OTHER SOURCE(S): MARPAT 140:146164
GI



I

AB Title compds. [I; R-R3 = H, OH, halo, (branched) alkyl, cycloalkyl, alkylcarbonyl, alkoxy, arylalkoxy, etc.; Z = O, S; n, m = 0-4; R4 = (branched) (saturated) (substituted) alkyl, aryl, arylalkyl, etc.], were prepared Thus, anthracene-9-carboxylic acid in DMF was treated successively with N-methylmorpholine, 1-(4-nitrophenyl)piperazine, and Py-BOP followed by stirring for 4 h at room temperature to give 79.7% 1-(4-nitrophenyl)-4-(anthracen-9-ylcarbonyl)piperazine. Anthracen-9-yl-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]methanone inhibited proliferation of different human tumor cells in XTT cytotoxicity test with EC50 = 0.047->3.16 μg/mL.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 3 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:60486 HCAPLUS
DOCUMENT NUMBER: 140:111430
TITLE: Preparation of (anthracenyl)(piperazinyl)methanones as antitumor agents
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Aue, Beate; Polymeropoulos, Emmanuel; Baasner, Silke; Schmidt, Peter
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004007470	A1	20040122	WO 2003-EP5156	20030516

W: AU, BR, BY, CA, CN, CO, GE, HR, HU, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, UA, UZ, YU, ZA

RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

EP 1521748	A1	20050413	EP 2003-763626		20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK					
CA 2435399	AA	20040117	CA 2003-2435399		20030717
US 2004110756	A1	20040610	US 2003-621590		20030717
PRIORITY APPLN. INFO.:			US 2002-396683P	P	20020717
			WO 2003-EP5156	W	20030516

OTHER SOURCE(S): MARPAT 140:111430

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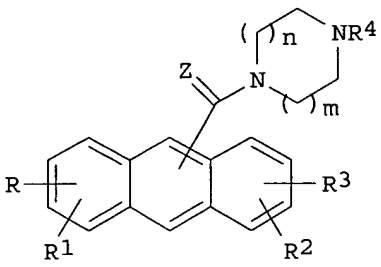

I

AB Title compds. [I; R-R3 = H, OH, halo, (branched) alkyl, cycloalkyl, alkylcarbonyl, alkoxy, arylalkoxy, etc.; Z = O, S; n, m = 0-4; R4 = (branched) (saturated) (substituted) alkyl, aryl, arylalkyl, etc.], were prepared Thus, anthracene-9-carboxylic acid in DMF was treated successively with N-methylmorpholine, 1-(4-nitrophenyl)piperazine, and Py-BOP followed by stirring for 4 h at room temperature to give 79.7% 1-(4-nitrophenyl)-4-(anthracen-9-ylcarbonyl)piperazine. Anthracen-9-yl-[4-(3,5-dimethoxyphenyl)piperazin-1-yl]methanone inhibited proliferation of different human tumor cells in XTT cytotoxicity test with EC50 = 0.047->3.16 μg/mL.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 4 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:107333 HCAPLUS

DOCUMENT NUMBER: 136:167288

TITLE: Preparation of N-(6-quinolinyl)-3-indolylglyoxylamides as antitumor agents

INVENTOR(S): **Emig, Peter**; Bacher, Gerald; Reichert, Dietmar; Baasner, Silke; Aue, Beate; Nickel, Bernd; Guenther, Eckhard

PATENT ASSIGNEE(S): Zentaris A.-G., Germany

SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002010152	A2	20020207	WO 2001-EP8644	20010726

WO 2002010152		A3	20020801		
W:	AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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DE 10037310		A1	20020207	DE 2000-10037310	20000728
US 2003100597		A1	20030529	US 2001-910140	20010720
CA 2354210		AA	20020128	CA 2001-2354210	20010726
EP 1309585		A2	20030514	EP 2001-969522	20010726
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
BR 2001012807		A	20030701	BR 2001-12807	20010726
JP 2004505075		T2	20040219	JP 2002-515883	20010726
NZ 524404		A	20040827	NZ 2001-524404	20010726
ZA 2003000584		A	20030718	ZA 2003-584	20030122
NO 2003000382		A	20030220	NO 2003-382	20030124
BG 107560		A	20031031	BG 2003-107560	20030214
PRIORITY APPLN. INFO.:				DE 2000-10037310 A	20000728
				WO 2001-EP8644 W	20010726

OTHER SOURCE(S): MARPAT 136:167288

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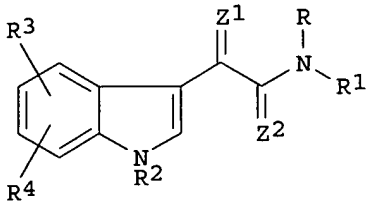


I

AB Title compds. [I; R = H, (substituted) alkyl, alkoxyalkyl, arylalkyloxycarbonyl, etc.; R1 = (substituted) (un)saturated and aromatic heterocyclyl especially (substituted) 2-, 3-, 4- and 8-quinolinyl and 2-, 3-, 4-quinolinylmethyl; R2 = H, (substituted) phenylalkyl, etc.; R3, R4 = H, OH, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, etc.; Z1 = O, S, H, OH; Z2 = O, S] and salts thereof were prepared Thus, (COCl)2 in ether was dropwise treated with 1-(4-chlorobenzyl)indole (preparation given) in ether under N2-atmosphere followed by reflux for 2 h and removal of solvent. The resulting reaction mixture in THF was dropwise treated with 6-amino-2-methylquinoline in THF followed by reflux for 4 h and then the reaction mixture was kept overnight at room temperature to give 77.3% N-(2-methyl-6-quinolinyl)-[1-(4-chlorobenzyl)indol-3-yl]glyoxylamide. The latter induced growth inhibition of e.g. human cervical carcinoma cell lines KB/HeLa with IC50 = 0.17 μM in a proliferation test.

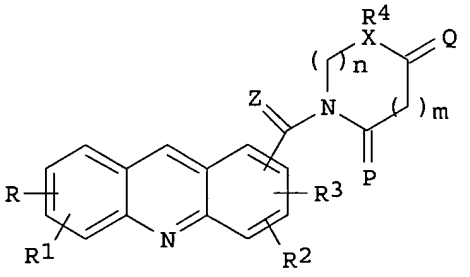
L25 ANSWER 5 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2002:90014 HCAPLUS
DOCUMENT NUMBER:	136:134791
TITLE:	Preparation of acridinylcarbonylpiperazines related compounds as anticancer drugs.
INVENTOR(S):	**Emig, Peter**; Guenther, Eckhard; Baasner, Silke; Bacher, Gerald; Beckers, Thomas; Aue, Beate
PATENT ASSIGNEE(S):	Zentaris A.-G., Germany
SOURCE:	PCT Int. Appl., 46 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008194	A1	20020131	WO 2001-EP8263	20010718
WO 2002008194	C1	20030508		
W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10035927	A1	20020307	DE 2000-10035927	20000721
EP 1301485	A1	20030416	EP 2001-969410	20010718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
BR 2001012591	A	20030722	BR 2001-12591	20010718
JP 2004504382	T2	20040212	JP 2002-514101	20010718
NZ 524155	A	20050429	NZ 2001-524155	20010718
CA 2353360	AA	20020121	CA 2001-2353360	20010720
US 2002132821	A1	20020919	US 2001-910142	20010720
US 6706722	B2	20040316		
ZA 2002010411	A	20030226	ZA 2002-10411	20021223
NO 2003000301	A	20030311	NO 2003-301	20030120
BG 107507	A	20030930	BG 2003-107507	20030130
PRIORITY APPLN. INFO.:			DE 2000-10035927 A	20000721
			WO 2001-EP8263 W	20010718

OTHER SOURCE(S): MARPAT 136:134791
GI



I

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, alkoxycarbonylamino, cyano, cyanoalkyl, CO2H, alkoxycarbonyl, CF3, etc.; Z = O, S; P, Q = O, H2; X = N, CR5; R5 = H, alkyl; m, n = 0-3; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.], were prepared Thus, acridine-9-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP, (1-benzotriazolyltripyrrolidinophosphoniu mhexafluorphosphate), and 1-(3,5-dimethoxyphenyl)piperazine in DMF. The mixture was stirred 12 h to give 84.2% 1-(3,5-dimethoxyphenyl)-4-(9-acridinylcarbonyl)piperazine. The latter inhibited KB/HeLa cell growth with IC50 <0.0003 μg/mL.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

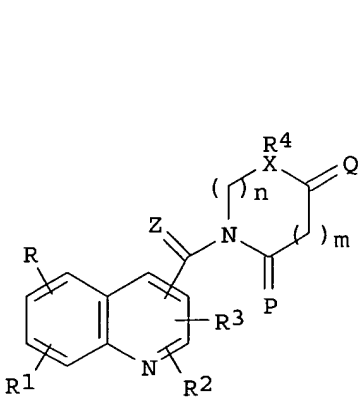
L25 ANSWER 6 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:90012 HCAPLUS

DOCUMENT NUMBER: 136:134790
TITLE: Preparation of quinolylcarbonylpiperazines and related compounds for treatment of tumors.
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Schmidt, Juergen; Nickel, Bernd; Kutscher, Bernhard
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

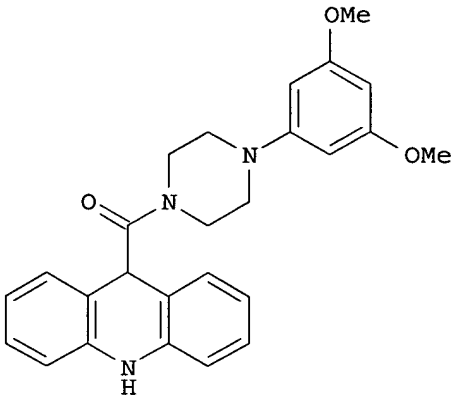
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008192	A1	20020131	WO 2001-EP8261	20010718
W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10035928	A1	20020307	DE 2000-10035928	20000721
EP 1305290	A1	20030502	EP 2001-957978	20010718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001012589	A	20030520	BR 2001-12589	20010718
JP 2004504381	T2	20040212	JP 2002-514099	20010718
NZ 524154	A	20050225	NZ 2001-524154	20010718
CA 2353369	AA	20020121	CA 2001-2353369	20010720
US 2002103214	A1	20020801	US 2001-910141	20010720
US 6890926	B2	20050510		
ZA 2002010180	A	20030212	ZA 2002-10180	20021217
NO 2003000298	A	20030120	NO 2003-298	20030120
BG 107508	A	20030930	BG 2003-107508	20030130
US 2004097530	A1	20040520	US 2003-713859	20031114
US 2004132747	A1	20040708	US 2003-741310	20031219
US 6936615	B2	20050830		
US 2005176744	A1	20050811	US 2005-105622	20050414

PRIORITY APPLN. INFO.:	DE 2000-10035928	A	20000721
	WO 2001-EP8261	W	20010718
	US 2001-910141	A3	20010720

OTHER SOURCE(S): MARPAT 136:134790
GI



I



II

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, cyano, CO2H, CF3, etc.; RR1, R2R3 = atoms to form condensed 6-membered aromatic rings; Z = O, S; X = N, CR5; R5 = H, alkyl; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.; P, Q = O, H2; m, n = 0-3], were prepared Thus, quinoline-4-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP (1-benzotriazolyltripyrrolidinopho sphoniumhexafluorophosphate), and 1-(3,5-dimethoxyphenyl)piperazine in DMF. The mixture was stirred 12 h to give 78.3% 1-(3,5-dimethoxyphenyl)-4-(4-quinolylcarbonyl)piperazine. Title compound (II) (D-43411) showed antiproliferative activity with IC50 <0.0003 μg/mL against SKOV-3 tumor cells.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

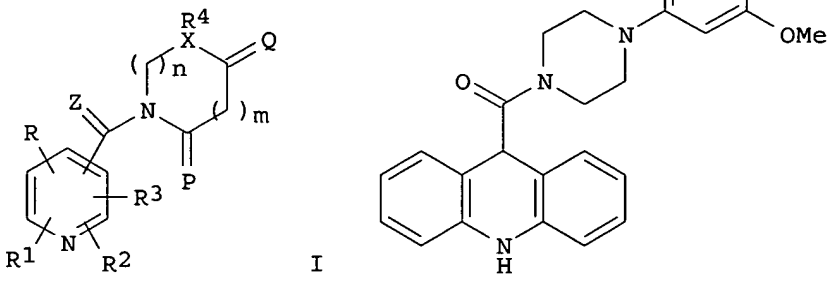
L25 ANSWER 7 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:90010 HCAPLUS
DOCUMENT NUMBER: 136:134789
TITLE: Preparation of pyridylcarbonylpiperazines and related compounds as anticancer drugs.
INVENTOR(S): **Emig, Peter**; Guenther, Eckhard; Schmidt, Juergen; Kutscher, Bernhard; Nickel, Bernd; Storch, Anita
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008190	A2	20020131	WO 2001-EP8262	20010718
WO 2002008190	A3	20020801		
W: AU, BG, BR, BY, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
DE 10035908	A1	20020307	DE 2000-10035908	20000721
EP 1305289	A2	20030502	EP 2001-960509	20010718
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, TR					
BR 2001012711	A	20030520	BR 2001-12711		20010718
JP 2004516243	T2	20040603	JP 2002-514097		20010718
CA 2353353	AA	20020121	CA 2001-2353353		20010720
US 2002111354	A1	20020815	US 2001-910139		20010720
US 6638935	B2	20031028			
ZA 2003000545	A	20030212	ZA 2003-545		20020121
NO 2003000302	A	20030207	NO 2003-302		20030120
BG 107506	A	20030930	BG 2003-107506		20030130
PRIORITY APPLN. INFO.:			DE 2000-10035908	A	20000721
			WO 2001-EP8262	W	20010718

OTHER SOURCE(S): MARPAT 136:134789

GI



I II

AB Title compds. [I; R-R3 = H, alkyl, cycloalkyl, alkylcarbonyl, alkoxy, halo, aralkoxy, NO2, amino, cyano, CO2H, alkoxycarbonyl, CF3, etc.; RR1, R2R3 = atoms to form fused 6-membered aromatic rings; Z = O, S; P, Q = O, H2; X = N, CR5; m, n = 0-3; R4 = (substituted) (unsatd.) alkyl, aryl, aralkyl, etc.], were prepared Thus, pyridine-4-carboxylic acid in DMF was treated with N-methylmorpholine, Py-BOP (1-benzotriazolyltripyrrolidinophosphonium hexafluorphosphate), 1-(3,5-dimethoxyphenyl)piperazine followed by stirring for 24 h to give 82.3% 1-(3,5-dimethoxyphenyl)-4-(4-pyridylcarbonyl)piperazine. Title compound (II) inhibited L1210 tumor cells with IC50<0.0003 μg/mL.

L25 ANSWER 8 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	2001:915607 HCAPLUS
DOCUMENT NUMBER:	136:193482
TITLE:	New small-molecule tubulin inhibitors
AUTHOR(S):	Bacher, G.; Beckers, T.; **Emig, P.**; Klenner, T.; Kutschert, B.; Nickel, B.
CORPORATE SOURCE:	IUPAC Commission, Research & Development Oncology, ASTA Medica AG, Frankfurt, 60314, Germany
SOURCE:	Pure and Applied Chemistry (2001), 73(9), 1459-1464 CODEN: PACHAS; ISSN: 0033-4545
PUBLISHER:	International Union of Pure and Applied Chemistry
DOCUMENT TYPE:	Journal; General Review
LANGUAGE:	English

AB A review. The variety of biol. agents directed toward the tubulin system exceeds those acting on DNA, making it an important target for cancer chemotherapy. However. the complicated chemical structures and restricted access to the natural resources, in combination with the development of

drug resistance, limit the first generation of natural products. Considerable efforts in the search and synthesis of new synthetic compds., such as small mol. tubulin inhibitors, gave access to novel potential/promising drugs. Among these substances, two series of novel, easily accessible indole classes were identified as tubulin-destabilizing agents. Owing to the synthetic nature, potent in vitro and in vivo antitumoral activity, and efficacy against multidrug-resistant (MDR) tumors, D-24851 and D-64131 have significant potential in cancer treatment.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 9 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:858552 HCAPLUS
DOCUMENT NUMBER: 136:247463
TITLE: Synthesis and pharmacological evaluation of (indol-3-yl)alkylamides as potent analgesic agents
AUTHOR(S): Fouchard, Fabienne; Marchand, Pascal; Le Baut, Guillaume; **Emig, Peter**; Nickel, Bernd
CORPORATE SOURCE: Laboratoires de Chimie Organique et de Chimie Therapeutique, Faculte de Pharmacie, Nantes, 44035, Fr.
SOURCE: Arzneimittel-Forschung (2001), 51(10), 814-824
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:247463
AB A series of (indol-3-yl)alkylamides was synthesized and evaluated for analgesic activity. Two N-(pyridin-4-yl)acetamides, bearing benzyl or 4-fluorobenzyl moieties in 1-position of indole ring, exhibited promising analgesic properties (ED50 = 8.1 and 11 mg/kg p.o., resp.). The two test compds. were tested for their anti-inflammatory activity by carrageenin-induced edema in rat paw test. 4-Fluorobenzyl derivative whose ID50 was 0.085 ± 0.021 mmol/kg was selected as a lead compound for further pharmacomodulation.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 10 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:790429 HCAPLUS
DOCUMENT NUMBER: 136:200078
TITLE: Synthesis and characterization of the biologically active 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide
AUTHOR(S): Knaack, Martin; **Emig, Peter**; Bats, Jan W.; Kiesel, Michael; Muller, Arndt; Gunther, Eckhard
CORPORATE SOURCE: Infracor GmbH, Hanau, 63457, Germany
SOURCE: European Journal of Organic Chemistry (2001), (20), 3843-3847
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:200078
AB The spectroscopic characterization of the new potent tubulin inhibitor 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide (D-24851), which is under preclin. development, is described. The synthesis was optimized and follows a straightforward route from the unsubstituted indole via 1-(4-chlorobenzyl)indole and 1-[(4-

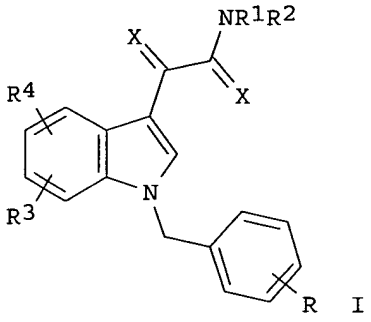
chlorophenyl)methyl]-α-oxo-N-4-pyridinyl-1H-indole-3-acetyl chloride to the target compound, D-24851. The structure was assigned by sophisticated NMR expts., for example a 1,1-ADEQUATE experiment, and X-ray crystallog.

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 11 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:467995 HCAPLUS
DOCUMENT NUMBER: 135:46111
TITLE: Preparation of N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamides as antitumor agents
INVENTOR(S): Guenther, Eckhard; **Emig, Peter**; Reichert, Dietmar; Le Baut, Guillaume; Nickel, Bernd; Bacher, Gerald
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: Ger. Offen., 10 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19962300	A1	20010628	DE 1999-19962300	19991223
US 2001014690	A1	20010816	US 2000-736431	20001215
US 6432987	B2	20020813		
CA 2395259	AA	20010705	CA 2000-2395259	20001219
WO 2001047913	A2	20010705	WO 2000-EP12947	20001219
W: AT, AU, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
BR 2000016712	A	20020903	BR 2000-16712	20001219
EP 1240157	A2	20020918	EP 2000-983349	20001219
EP 1240157	B1	20040211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR				
JP 2003519137	T2	20030617	JP 2001-549383	20001219
AT 259364	E	20040215	AT 2000-983349	20001219
AU 772745	B2	20040506	AU 2001-20119	20001219
PT 1240157	T	20040630	PT 2000-983349	20001219
NZ 519977	A	20040827	NZ 2000-519977	20001219
ES 2215768	T3	20041016	ES 2000-983349	20001219
NZ 533731	A	20050324	NZ 2000-533731	20001219
ZA 2002004896	A	20021220	ZA 2002-4896	20020619
NO 2002003039	A	20020809	NO 2002-3039	20020621
BG 106924	A	20030430	BG 2002-106924	20020716
PRIORITY APPLN. INFO.:			DE 1999-19962300 A	19991223
			WO 2000-EP12947 W	20001219

OTHER SOURCE(S): MARPAT 135:46111
GI



AB Title compds. [I; R1 = H, (substituted) alkyl, benzyloxycarbonyl, t-butoxycarbonyl, OAc; R2 = (substituted) Ph, pyridinyl, pyrimidinyl, etc.; or R1R2 = (substituted) (homo)piperazinyl; R3, R4 = H, alkyl, cycloalkyl, alkanoyl, alkoxy, halo, PhCH2O, NO2, amino, etc.; R = NO2, amino, (di)alkylamino, cycloalkylamino, phenylalkylamino, (hetero)aroylamino, etc.; X = O, S] were prepared as antitumor agents (no data). Thus, (COCl)2 in Et2O at 0° was treated dropwise with indole in Et2O and refluxed for 3 h followed by dropwise addition of 4-aminopyridine in THF at 5° and reflux over night to give 43.3% N-(pyridin-4-yl) (indol-3-yl)glyoxylamide. The product was treated with 4-nitrobenzyl chloride to give 64% N-(pyridin-4-yl) [1-(4-nitrobenzyl)indol-3-yl]glyoxylamide (D-68836). The latter was subjected to catalytic hydrogenation to give 94% N-(pyridin-4-yl) [1-(4-aminobenzyl)indol-3-yl]glyoxylamide (D-68838). D-68838 was said to inhibit polymerization of tubulin.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 12 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:247170 HCAPLUS
DOCUMENT NUMBER: 134:261240
TITLE: Indolyl-3-glyoxylic acid derivatives comprising therapeutically valuable properties
INVENTOR(S): Nickel, Bernd; Klenner, Thomas; Bacher, Gerald; Beckers, Thomas; **Emig, Peter**; Engel, Juergen; Bruyneel, Erik; Kamp, Guenter; Peters, Kirsten
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022954	A2	20010405	WO 2000-EP9390	20000926
WO 2001022954	A3	20020328		
W: AU, BG, BR, BY, CA, CN, CZ, DZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19946301	A1	20010419	DE 1999-19946301	19990928

US 2003114511	A1	20030619	US 2000-492531		20000127
US 6693119	B2	20040217			
CA 2386069	AA	20010405	CA 2000-2386069		20000926
EP 1218006	A2	20020703	EP 2000-967789		20000926
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
JP 2003510274	T2	20030318	JP 2001-526166		20000926
EE 200200169	A	20030415	EE 2002-169		20000926
BR 2000014378	A	20030729	BR 2000-14378		20000926
NZ 517988	A	20041029	NZ 2000-517988		20000926
NO 2002001367	A	20020522	NO 2002-1367		20020319
ZA 2002002556	A	20030704	ZA 2002-2556		20020402
BG 106639	A	20021229	BG 2002-106639		20020423
US 2004171668	A1	20040902	US 2003-686809		20031017
PRIORITY APPLN. INFO.:			DE 1999-19946301	A	19990928
			DE 1998-19814838	A	19980402
			US 1999-285058	A2	19990402
			US 2000-492531	A1	20000127
			WO 2000-EP9390	W	20000926

OTHER SOURCE(S): MARPAT 134:261240

AB The invention relates to the use of N-substituted indol-3- glyoxylamides of for treating tumors, in particular, in cases of drug resistance and metastatic carcinoma, and as angiogenesis inhibitors having distinctly fewer side effects, in particular, distinctly lower neurotoxicity. The invention also relates to medicaments containing the inventive compds.

L25 ANSWER 13 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:58000 HCAPLUS

DOCUMENT NUMBER: 134:290069

TITLE: D-24851, a novel synthetic microtubule inhibitor, exerts curative antitumoral activity in vivo, shows efficacy toward multidrug-resistant tumor cells, and lacks neurotoxicity

AUTHOR(S): Bacher, Gerald; Nickel, Bernd; **Emig, Peter**; Vanhoefer, Udo; Seeber, Siegfried; Shandra, Alexei; Klenner, Thomas; Beckers, Thomas

CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt am Main, 60314, Germany

SOURCE: Cancer Research (2001), 61(1), 392-399
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB N-(pyridin-4-yl)-[1-(4-chlorbenzyl)indol-3-yl]glyoxylamide (D-24851) is a novel synthetic compound that was identified in a cell-based screening assay to discover cytotoxic drugs. D-24851 destabilizes microtubules and blocks cell cycle transition specifically at G2-M phase. The binding site of D-24851 does not overlap with the tubulin binding sites of known microtubule-destabilizing agents like vincristine or colchicine. In vitro, D-24851 has potent cytotoxic activity toward a panel of established human tumor cell lines including SKOV3 ovarian cancer, U87 glioblastoma, and ASPC-1 pancreatic cancer cells. In vivo, oral D-24851 treatment induced complete tumor regressions (cures) in rats bearing Yoshida AH13 sarcomas. Of importance is that the administration of curative doses of D-24851 to the animals revealed no systemic toxicity in terms of body weight loss and neurotoxicity in contrast to the administration of paclitaxel or vincristine. Interestingly, multidrug-resistant cell lines generated by vincristine-driven selection or transfection with the Mr 170,000 P-glycoprotein encoding cDNA were rendered resistant toward paclitaxel, vincristine, or doxorubicin but not towards D-24851 when compared with the

parental cells. Because of its synthetic nature, its oral applicability, its potent in vitro and in vivo antitumoral activity, its efficacy against multidrug-resistant tumors, and the lack of neurotoxicity, D-24851 may have significant potential for the treatment of various malignancies.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

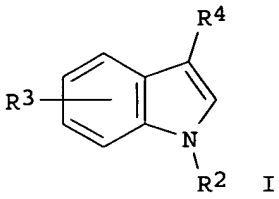
L25 ANSWER 14 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:659229 HCAPLUS
DOCUMENT NUMBER: 131:271807
TITLE: Preparation of indolylglyoxylamides as antitumor agents
INVENTOR(S): Nickel, Bernd; Szelenyi, Istvan; Schmidt, Jurgen; **Emig, Peter**; Reichert, Dietmar; Gunther, Eckhard; Brune, Kay
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951224	A1	19991014	WO 1999-EP1918	19990322
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19814838	A1	19991014	DE 1998-19814838	19980402
DE 19814838	C2	20010118		
CA 2326833	AA	19991014	CA 1999-2326833	19990322
AU 9929349	A1	19991025	AU 1999-29349	19990322
AU 768510	B2	20031218		
BR 9909902	A	20001226	BR 1999-9902	19990322
EP 1071420	A1	20010131	EP 1999-910372	19990322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200002853	T2	20010221	TR 2000-200002853	19990322
EE 200000581	A	20020215	EE 2000-581	19990322
EE 4354	B1	20041015		
JP 2002510622	T2	20020409	JP 2000-541995	19990322
NZ 507084	A	20031031	NZ 1999-507084	19990322
US 6232327	B1	20010515	US 1999-285058	19990402
US 2003114511	A1	20030619	US 2000-492531	20000127
US 6693119	B2	20040217		
NO 2000004916	A	20001201	NO 2000-4916	20000929
HR 2000000643	A1	20010430	HR 2000-643	20001002
BG 104849	A	20010531	BG 2000-104849	20001012
ZA 2000006150	A	20010111	ZA 2000-6150	20001031
US 2003023093	A1	20030130	US 2001-810604	20010319
HK 1036408	A1	20050218	HK 2001-107405	20011024
US 2003195360	A1	20031016	US 2002-309204	20021204
US 2004171668	A1	20040902	US 2003-686809	20031017

PRIORITY APPLN. INFO.:		
DE 1998-19814838	A	19980402
WO 1999-EP1918	W	19990322
US 1999-285058	A1	19990402
DE 1999-19946301	A	19990928

US 2000-492531 A1 20000127
US 2001-810604 A1 20010319

OTHER SOURCE(S): MARPAT 131:271807
GI



I

AB Title compds. [I; R2 = H or (un)substituted alkyl; R3 = H or 1 or 2 of halo, alkyl, alkoxy, etc.; R4 = C(:X)C(:X)NRR1; R = H, (un)substituted alkyl, CO2CH2Ph, etc.; R1 = (un)substituted Ph, -pyridyl, -pyrimidyl, etc.; RR1 = (CH2CH2)2NR7; R7 = alkyl, Ph, CHPh2, etc.; X = O or S] were prepared Thus, indole was N-alkylated by 4-FC6H4CH2Cl and the product acylated by (COCl)2 to give, after 4-aminopyridine amidation, I (R2 = CH2C6H4F-4, R3 = H, R4 = COCONHR1, R1 = 4-pyridyl). Data for biol. activity of I were given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 15 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:65867 HCAPLUS
DOCUMENT NUMBER: 130:223153
TITLE: New N-(Pyridin-4-yl)-(indol-3-yl)acetamides and Propanamides as Antiallergic Agents
AUTHOR(S): Menciu, Cecilia; Duflos, Muriel; Fouchard, Fabienne; Le Baut, Guillaume; **Emig, Peter**; Achterrath, Ute; Szelenyi, Istvan; Nickel, Bernd; Schmidt, Juergen; Kutscher, Bernhard; Guenther, Eckhardt
CORPORATE SOURCE: Department of Organic Chemistry and Medicinal Chemistry, Faculty of Pharmacy, Nantes, 44035, Fr.
SOURCE: Journal of Medicinal Chemistry (1999), 42(4), 638-648
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of new N-(pyridin-4-yl)-(indol-3-yl)alkylamides has been prepared in the search of novel antiallergic compds. Synthesis of the desired Et (2-methyindol-3-yl)acetates was achieved by indolization under Fischer conditions; Japp-Klingemann method followed by 2-decarboxylation afforded the Et (indol-3-yl)alkanoates. Amidification was successfully carried out by condensation of the acids or their N-aryl(methyl) derivs. with 4-aminopyridine promoted by 2-chloro-1-methylpyridinium iodide. Efforts to improve the antiallergic potency of the title series by variation of the indole substituents (R1, R2, R) and the length of the alkanoic chain (n = 1, 2, 3) led to the selection of N-(pyridin-4-yl)-[1-(4-fluorobenzyl)indol-3-yl]acetamide (I), out of 41 compds. This amide was 406-fold more potent than astemizole in the ovalbumin-induced histamine release assay, using guinea pig peritoneal mast cells, with an IC50 = 0.016 μM. Its inhibitory activity in IL-4 production test from Th-2 cells was identical to that of the reference histamine antagonist (IC50 = 8.0 μM) and twice higher in IL-5 assay: IC50 = 1.5 and 3.3 μM, resp. In vivo antiallergic activity evaluation confirmed efficiency of I in sensitized

guinea pig late phase eosinophilia inhibition, after parenteral and oral administration at 5 and 30 mg/kg, resp. Its efficiency in inhibition of microvascular permeability was assessed in two rhinitis models; ovalbumin and capsaicin-induced rhinorrhea could be prevented after topical application of submicromolar concns. of 45 (IC50 = 0.25 and 0.30 μM); and it also exerted significant inhibitory effect in the first test after i.v. and oral administration, with ID50 = 0.005 and 0.46 mg/kg.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 16 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:46386 HCAPLUS
DOCUMENT NUMBER: 130:100782
TITLE: Polymorphism and desolvation of flupirtine maleate
AUTHOR(S): Landgraf, Karl-Friedrich; Olbrich, Alfred; Pauluhn, Siegfried; **Emig, Peter**; Kutscher, Bernhard; Stange, Hans
CORPORATE SOURCE: ASTA Medica A.-G., Dresden, Germany
SOURCE: European Journal of Pharmaceutics and Biopharmaceutics (1998), 46(3), 329-337
CODEN: EJPBEL; ISSN: 0939-6411
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crystallizates of the analgesic agent flupirtine maleate (Katadolon; ASTA Medica, Dresden, Germany) obtained from isopropanol are examined by x-ray diffractometry, polarization microscopy and thermoanal. Depending on the crystallizing conditions, the modifications A and B as well as an isopropanol solvate are observed The inversion temperature A → B of the enantiotropic modifications is 164° (differential scanning calorimetry (DSC) onset). During thermal desolvation, modification B is formed well below the inversion temperature In concentrated isopropanol suspensions, the solvate and modification B are rapidly transformed into modification A. It is shown how phase-pure products consisting of modification A, which is better wettable with water and stable at room temperature, can be obtained.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 17 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:709053 HCAPLUS
DOCUMENT NUMBER: 129:316153
TITLE: Preparation of pure flupirtin maleate and its A crystal modification.
INVENTOR(S): Olbrich, Alfred; **Emig, Peter**; Kutscher, Bernhard; Landgraf, Karl-Friedrich; Pauluhn, Siegfried; Stange, Hans
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847872	A1	19981029	WO 1998-EP2118	19980411

W: AU, BR, CA, CN, CZ, HU, IS, JP, NO, PL, RU, SK
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,

PT, SE

DE 19716984	A1	19981029	DE 1997-19716984	19970423
AU 9873346	A1	19981113	AU 1998-73346	19980411
EP 977736	A1	20000209	EP 1998-920511	19980411
EP 977736	B1	20030924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001523236	T2	20011120	JP 1998-544940	19980411
AT 250579	E	20031015	AT 1998-920511	19980411
PT 977736	T	20040227	PT 1998-920511	19980411
ES 2207832	T3	20040601	ES 1998-920511	19980411
ZA 9803376	A	19980703	ZA 1998-3376	19980422
US 5959115	A	19990928	US 1998-64790	19980423
PRIORITY APPLN. INFO.:			DE 1997-19716984 A	19970423
			WO 1998-EP2118 W	19980411

AB Flupirtin maleate (I) was prepared by hydrogenation of 2-amino-3-nitro-6-(4-fluorobenzylamino)pyridine (II) using Raney Ni, acylation with EtO2CCl, and treatment of the resulting flupirtin with maleic acid. Thus, II in Me2CHOH was hydrogenated over Raney Ni at 65° and 5 bar H2; EtO2CCl and Et3N were added followed by stirring at 60°, filtration at 50-60° into a solution of maleic acid in H2O to precipitate I (89.6% yield). I A crystal modification was obtained by stirring I A and B crystal modification mixture in Me2CHOH.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

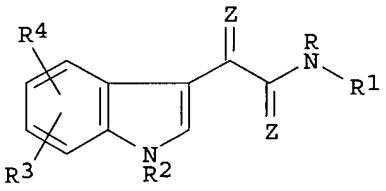
L25 ANSWER 18 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:175908 HCAPLUS
DOCUMENT NUMBER: 128:217285
TITLE: Preparation of new, N-substituted indole-3-glyoxylamides as antiasthmatics, antiallergic agents and immunosuppressants/immunomodulators
INVENTOR(S): Lebaut, Guillaume; Menciu, Cecilia; Kutscher, Bernhard; **Emig, Peter**; Szelenyi, Stefan; Brune, Kay
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9809946	A1	19980312	WO 1997-EP4474	19970816
W: AU, BR, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SG, SK, TR, UA				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19636150	A1	19980312	DE 1996-19636150	19960906
AU 9740158	A1	19980326	AU 1997-40158	19970816
AU 726521	B2	20001109		
EP 931063	A1	19990728	EP 1997-937586	19970816
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1227542	A	19990901	CN 1997-197128	19970816
BR 9712808	A	19991123	BR 1997-12808	19970816
JP 2000505098	T2	20000425	JP 1998-512167	19970816
JP 3296437	B2	20020702		
NZ 334476	A	20000526	NZ 1997-334476	19970816

IL 127798	A1	20030731	IL 1997-127798		19970816
CN 1496980	A	20040519	CN 2002-2002132061		19970816
RU 2237661	C2	20041010	RU 1999-106782		19970816
ZA 9707475	A	19980219	ZA 1997-7475		19970820
CA 2215013	AA	19980306	CA 1997-2215013		19970904
CA 2215013	C	20020305			
US 6008231	A	19991228	US 1997-925326		19970908
TW 550256	B	20030901	TW 1997-86112985		19970930
NO 9901071	A	19990304	NO 1999-1071		19990304
NO 314725	B1	20030512			
US 6344467	B1	20020205	US 1999-409263		19990930
US 2002161025	A1	20021031	US 2002-58836		20020130
NO 2003000481	A	19990304	NO 2003-481		20030130
US 2003207892	A1	20031106	US 2003-402931		20030401
US 6919344	B2	20050719			
PRIORITY APPLN. INFO.:			DE 1996-19636150	A	19960906
			WO 1997-EP4474	W	19970816
			US 1997-925326	A3	19970908
			US 1999-409263	A3	19990930
			US 2002-58836	B1	20020130

OTHER SOURCE(S): MARPAT 128:217285
GI



I

AB The title compds. [I; R = H, (un)substituted C1-6 alkyl; R1 = (un)substituted Ph, pyridyl, pyrimidinyl, etc.; RR1 = atoms to close (N-substituted) piperazine ring; R2 = H, (un)substituted C1-6 alkyl, (un)substituted benzoyl; R3, R4 = H, OH, C1-6 alkyl, C3-7 cycloalkyl, halo, NO2, amino, benzyloxy, etc.; Z = O, S] and their acid salts were prepared, e.g., by N-alkylation of indoles with R2-bearing reactants followed by acylation with a dicarbonyl halide and amidation of the remaining acid halide function. For example, a title compound I (R = R3 = R4 = H, R1 = 4-pyridyl, R2 = 4-FC6H4CH2, Z = O) (preparation by benzylation of indole with 4-FC6H4CH2Cl, acylation of the intermediate with (COCl)2 and amidation of the acyl chloride with 4-aminopyridine given) at 10 mg/kg i.p. in guinea pigs gave 55.4% inhibition of allergen-induced late-phase eosinophilia, vs. 47.0 for cyclosporin A.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L25 ANSWER 19 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:534403 HCAPLUS
DOCUMENT NUMBER: 125:221765
TITLE: Ring-rearrangement during the Mitsunobu alkylation of phthalazinones and indazolols
AUTHOR(S): Knaack, Martina; Fleischhauer, Ilona; Charpentier, Patricia; **Emig, Peter**; Kutscher, Bernhard; Mueller, Arndt
CORPORATE SOURCE: Degussa A.-G., Hanau, D-63403, Germany
SOURCE: Liebigs Annalen (1996), (9), 1477-1482

CODEN: LANAEM; ISSN: 0947-3440
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The Mitsunobu alkylation of substituted phthalazinones and indazolols with cyclic hydroxy- and hydroxymethyl-substituted amines was investigated. In addition to the expected derivs. ring-narrowed and ring-enlarged rearrangement products were isolated and characterized by NMR. The occurrence of these products is explained by the existence of a bicyclic intermediate. The results of the reaction of phthalazinones with optically active amine compds. show a stereospecific reaction mechanism. The reaction of the phthalazinones leads to N-substituted products, while in the case of the indazolols O-substituted derivs. were isolated. A postulated bicyclic intermediate, 1-methyl-1-azoniabicyclo[3.2.0]heptane, was synthesized as chloride.

L25 ANSWER 20 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:273624 HCAPLUS
DOCUMENT NUMBER: 124:316986
TITLE: Preparation of N-benzylindoles and -benzopyrazoles with antiasthmatic, antiallergic, antiinflammatory, and immunomodulating activity.
INVENTOR(S): Le Baut, Guillaume; Fouchard, Fabienne; Kutscher, Bernhard; **Emig, Peter**; Schmidt, Juergen; Szelenyi, Stefan; Fleischhauer, Ilona
PATENT ASSIGNEE(S): Asta Medica Ag, Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19511916	A1	19960208	DE 1995-19511916	19950331
CA 2195850	AA	19960215	CA 1995-2195850	19950720
WO 9604266	A2	19960215	WO 1995-EP2867	19950720
WO 9604266	A3	19960517		
W: AU, BR, BY, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, RU, SI, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9531626	A1	19960304	AU 1995-31626	19950720
EP 775131	A2	19970528	EP 1995-927679	19950720
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10503501	T2	19980331	JP 1995-506137	19950720
TW 434227	B	20010516	TW 1995-84107752	19950726
ZA 9506382	A	19960313	ZA 1995-6382	19950731
IL 114795	A1	19991130	IL 1995-114795	19950801
EG 21559	A	20011231	EG 1995-644	19950801
NO 9700412	A	19970227	NO 1997-412	19970130
FI 9701334	A	19970401	FI 1997-1334	19970401
US 5965582	A	19991012	US 1997-776616	19970512
PRIORITY APPLN. INFO.:			DE 1994-4427393 A1	19940803
			DE 1995-19511916 A	19950331
			WO 1995-EP2867 W	19950720

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. [I, II; R1, R10, R11, R12 = alkyl, cycloalkyl, alkoxy, (substituted) aryl, aroyl, quinolylmethyl, etc.; R2, R3 = H, alkyl, cycloalkyl, NO2, amino; R4 = H, alkyl, cycloalkyl; R5 = N-alkyl-2-pyrrolidinyl, amino; W = CH, NH; Y = O, S; X = CH, N, bond], were prepared Thus, title compound (III), prepared from indole-3-acetic acid by benzylation with 4-fluorobenzyl chloride, partial hydrolysis with NaOH in H2O/EtOH, and amidation with 4-aminopyridine/DCC, inhibited allergen-induced histamine release in rat mast cells with IC50 = 0.016 μmol/L.

L25 ANSWER 21 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:605183 HCAPLUS
DOCUMENT NUMBER: 121:205183
TITLE: Synthesis and Quantitative Structure-Activity Relationships of Anticonvulsant 2,3,6-Triaminopyridines
AUTHOR(S): Seydel, Joachim K.; Schaper, Klaus-J.; Coats, Eugene A.; Cordes, Hans P.; **Emig, Peter**; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel E.
CORPORATE SOURCE: Borstel Research Institute, Borstel, 23845, Germany
SOURCE: Journal of Medicinal Chemistry (1994), 37(19), 3016-22
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
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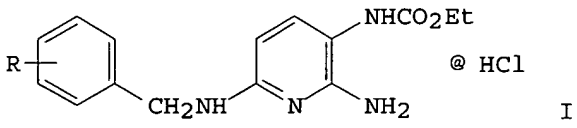


I

AB The synthesis of 2,3,6-triaminopyridine derivs., , e.g. I (R = H, 3-F, 4-Cl, 4-Ac, 4-NHAc, 2-Me, 2-OH, 4-CF3, 2,4-F2, 2,4-Me2, 2,6-Me2 2,4,6-Me3), representing a unique chemical structure for anticonvulsants, is described. The synthetic program was performed (a) to identify more potent analogs, (b) to determine structural properties controlling potency as well as neurotoxicity, and (c) to reduce the requirements for animal testing. As a result, besides other structural properties, the overall mol. lipophilicity (log k', octanol-coated column) explained changes in anticonvulsant potency and neurotoxicity. Mimicking the interaction of the amphiphilic triaminopyridines with biol. membranes, NMR expts. in the presence of lecithin vesicles were conducted in order to measure the phospholipid-binding parameter log Δ(1/T2). Replacement of log k' with log Δ(1/T2) in the correlation anal. afforded a more significant equation describing the anticonvulsant activity of 21 derivs.

L25 ANSWER 22 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:569743 HCAPLUS
DOCUMENT NUMBER: 121:169743
TITLE: QSAR analysis of time- and dose-dependent in vivo drug effects using artificial neural networks
AUTHOR(S): Schapper, Klaus-Juergen; Wiese, Michael; Dieter,

Reinhold; **Emig, Peter**; Engel, Juergen; Kutscher, Bernhard; Polymeropoulos, Emmanuel E.
CORPORATE SOURCE: Borstel Res. Inst., Borstel, D-2061, Germany
SOURCE: Trends QSAR Mol. Modell. 92, Proc. Eur. Symp. Struct.-Act. Relat.: QSAR Mol. Modell., 9th (1993), Meeting Date 1992, 546-9. Editor(s): Wermuth, Camille-Georges. ESCOM: Leiden, Neth.
CODEN: 59XTAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB QSAR anal. of time- and dose-dependent in vivo anticonvulsant activities of triaminobenzenes was carried out. Property-dependent activities were estimated Complete dos-response curves were obtained.

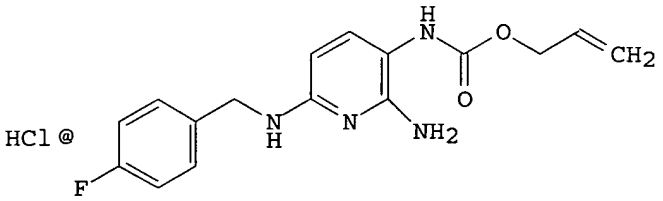
L25 ANSWER 23 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:426878 HCAPLUS
DOCUMENT NUMBER: 121:26878
TITLE: Pharmaceutical composition consisting of flupirtine and morphine for the treatment of pain and to avoid a morphine addiction
INVENTOR(S): Nickel, Bernd; Lobisch, Michael; Szelenyi, Stefan; Engel, Juergen; **Emig, Peter**; Pergande, Gabriela
PATENT ASSIGNEE(S): ASTA Medica AG, Germany
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 595311	A1	19940504	EP 1993-117472	19931028
EP 595311	B1	19970122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 4236752	A1	19940505	DE 1992-4236752	19921030
US 5521178	A	19960528	US 1993-141678	19931027
AT 147979	E	19970215	AT 1993-117472	19931028
ES 2099344	T3	19970516	ES 1993-117472	19931028
CA 2102072	AA	19940501	CA 1993-2102072	19931029
CA 2102072	C	20050104		
BR 9304431	A	19940607	BR 1993-4431	19931029
JP 06211663	A2	19940802	JP 1993-271730	19931029
JP 3665354	B2	20050629		
HU 66085	A2	19940928	HU 1993-3089	19931029
HU 219907	B	20010928		

PRIORITY APPLN. INFO.: DE 1992-4236752 A 19921030
AB Coadministration of flupirtine and morphine results in additive analgesic activity, reduced dependence on morphine, and no development of tolerance to flupirtine. Thus, the excitation, rearing behavior, and rigidity seen in rats after withdrawal from morphine in long-term expts. were markedly less in rats which had been injected with morphine and flupirtine. A preferred dosage form was a tablet containing 50-500 mg flupirtine and 10-250 mg morphine as salts.

L25 ANSWER 24 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:560063 HCAPLUS
DOCUMENT NUMBER: 119:160063
TITLE: New triaminopyridines with a central analgesic

activity
AUTHOR(S): **Emig, P.**; Nickel, B.; Weischer, C.-H.; Szelenyi, I.; Engel, J.
CORPORATE SOURCE: Forschung Asta Med. AG, Frankfurt/Main, Germany
SOURCE: Arzneimittel-Forschung (1993), 43(6), 627-31
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
GI



I

AB 2-Amino-3-[[[(3-propenyl)oxy]carbonyl]amino]-6-[(4-fluorobenzyl)amino]pyridine hydrochloride [D-19050; 2-propenyl [2-amino-6-[[(4-fluorophenyl)methyl]amino]-3-pyridinyl]carbamate] (I) is a centrally and peripherally acting analgesic with rapid onset, long duration of action and a good therapeutic range. D-19050 can be obtained in a 5-step-preparation starting from 2,6-dichloropyridine. I is a flupirtine analog.

L25 ANSWER 25 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:120908 HCAPLUS
DOCUMENT NUMBER: 116:120908
TITLE: Flupirtine as spasmolytic
INVENTOR(S): Lobisch, Michael; Venhaus, Ralph; Nickel, Bernd; Szelenyi, Istvan; Engel, Juergen; **Emig, Peter**
PATENT ASSIGNEE(S): Asta Pharma A.-G., Germany
SOURCE: Ger. Offen., 7 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4122166	A1	19920116	DE 1991-4122166	19910704
IN 172468	A	19930814	IN 1991-CA421	19910604
EP 467164	A2	19920122	EP 1991-111124	19910704
EP 467164	A3	19920415		
EP 467164	B1	19960131		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 659410	A2	19950628	EP 1995-101189	19910704
EP 659410	A3	19951025		
EP 659410	B1	20011017		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 133564	E	19960215	AT 1991-111124	19910704
ES 2082887	T3	19960401	ES 1991-111124	19910704
AT 206919	E	20011115	AT 1995-101189	19910704
ES 2164111	T3	20020216	ES 1995-101189	19910704
CZ 280879	B6	19960417	CZ 1991-2101	19910708

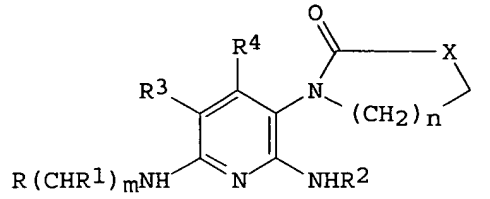
SK 279567	B6	19990111	SK 1991-2101	19910708
RO 108220	B1	19940331	RO 1991-147972	19910709
US 5162346	A	19921110	US 1991-726408	19910710
CA 2046943	AA	19920115	CA 1991-2046943	19910712
CA 2046943	C	19960312		
NO 9102758	A	19920115	NO 1991-2758	19910712
AU 9180403	A1	19920116	AU 1991-80403	19910712
AU 634073	B2	19930211		
ZA 9105466	A	19920429	ZA 1991-5466	19910712
HU 59313	A2	19920528	HU 1991-2359	19910712
HU 206973	B	19930301		
IL 98810	A1	19960119	IL 1991-98810	19910712
RU 2070408	C1	19961220	RU 1991-5001150	19910712
CN 1058716	A	19920219	CN 1991-104030	19910713
CN 1070700	B	20010912		
KR 182811	B1	19990501	KR 1991-11967	19910713
JP 05032627	A2	19930209	JP 1991-188472	19910729
US 5284861	A	19940208	US 1992-890730	19920601
LV 10048	B	19950620	LV 1992-173	19921027
LT 3593	B	19951227	LT 1993-919	19930903
PRIORITY APPLN. INFO.:			DE 1990-4022442	A1 19900714
			EP 1991-111124	A3 19910704
			US 1991-726408	A3 19910710

AB Flupirtine (I) is a spasmolytic for muscles. I may be used for increasing the tonus of skeletal muscles in parkinsonism, optionally in combination with known drugs for the treatment of parkinsonism, such as (-)-deprenyl, biperiden or L-DOPA. I.p. administration of 5 mg I + 5 mg L-DOPA/kg decreased in vivo the reserpine-induced rigidity of the rat flexor muscle.

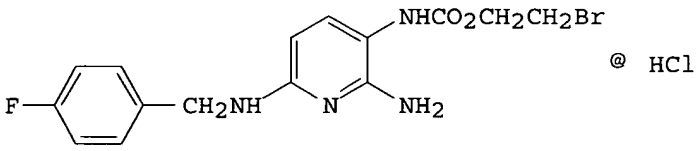
L25 ANSWER 26 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:235286 HCAPLUS
DOCUMENT NUMBER: 112:235286
TITLE: Preparation of (aminopyridyl)oxazolidinones and their analogs as antiepileptics
INVENTOR(S): Engel, Juergen; **Emig, Peter**; Nickel, Bernd; Szelenyi, Istvan
PATENT ASSIGNEE(S): Asta Pharma A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3915184	A1	19891130	DE 1989-3915184	19890510
EP 343429	A1	19891129	EP 1989-108369	19890510
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8902326	A	19891117	DK 1989-2326	19890512
AU 8934819	A1	19891116	AU 1989-34819	19890515
JP 02017186	A2	19900122	JP 1989-120578	19890516
US 4923858	A	19900508	US 1989-352287	19890516
PRIORITY APPLN. INFO.:			DE 1988-3816629	A1 19880516

OTHER SOURCE(S): CASREACT 112:235286; MARPAT 112:235286
GI



I



II

AB The title compds. [I; R = (substituted) aryl; R1, R2 = H, alkyl; R3, R4 = H, alkyl, OH, alkoxy, etc.; X = O, S, (substituted) imino; m, n = 1, 2, 3] are prepared Bromoethyl pyridylcarbamate II in EtOH was treated with NH3 in EtOH at room temperature for 24 h to give I [R = p-FC6H4, R1-R4 = H, X = O, m = n = 1]. In an example using the maximum elec. shock test, the ED50 for I (no specific compound mentioned) was 56 mg/kg in mice. Capsules and suppositories containing I were formulated.

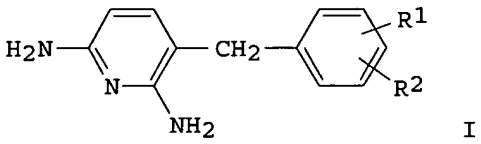
L25 ANSWER 27 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:453587 HCAPLUS
DOCUMENT NUMBER: 111:53587
TITLE: Determination of total bilirubin in serum and test strip determination for bilirubinemia, urobilinogenuria, and proteinuria: interference form the analgesic flupirtin
AUTHOR(S): Thomas, L.; Riethmueller-Winzen, H.; Niebch, G.; **Emig, P.**; Harleman, J. H.
CORPORATE SOURCE: Zentrallab., Krankenhaus Nordwest, Frankfurt/Main, D-6900/90, Fed. Rep. Ger.
SOURCE: Laboratoriumsmedizin (1989), 13(4), 136-41
CODEN: LABOD3; ISSN: 0342-3026
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Test strips (Ames-N-multistix, Combur-9-Test, Rapignost-Total-Screen) gave false-pos. results for bilirubin (I), urobilinogen (II), and protein (III) detns. in human urine in the presence of flupirtine (IV), either following in vitro spiking of samples or after daily oral administration of the drug to patients. For I and II detns., strongly colored azo-type reactions with the indicator reagents were observed; for III detns. the reason for this interference was not found, although expts. indicated that the biuret determination of III was not influenced by IV. Test-strip detns. of total blood serum I were also influenced by IV (i.e. they indicated increased I values in a IV dose-dependent manner) which depended upon assay system used, but at the maximum serum levels of IV expected, this interference was clin. insignificant.

L25 ANSWER 28 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:492815 HCAPLUS
DOCUMENT NUMBER: 109:92815
TITLE: Preparation of 2,6-diamino-3-(halobenzyl)pyridines as analgesics and antipyretics

INVENTOR(S): **Emig, Peter**; Engel, Juergen; Scheffler, Gerhard; Weischer, Carl Heinrich; Nickel, Bernd
PATENT ASSIGNEE(S): Asta Pharma A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 5 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3637829	A1	19880511	DE 1986-3637829	19861106
CN 87106966	A	19880831	CN 1987-106966	19871019
EP 266711	A1	19880511	EP 1987-116036	19871031
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8704875	A	19880507	FI 1987-4875	19871104
DD 270903	A5	19890816	DD 1987-308667	19871104
DD 276280	A5	19900221	DD 1987-323143	19871104
PL 149462	B1	19900228	PL 1987-268592	19871104
DK 8705814	A	19880507	DK 1987-5814	19871105
NO 8704617	A	19880509	NO 1987-4617	19871105
AU 8780826	A1	19880512	AU 1987-80826	19871105
AU 596708	B2	19900510		
JP 63132875	A2	19880604	JP 1987-278411	19871105
ZA 8708324	A	19880629	ZA 1987-8324	19871105
HU 45502	A2	19880728	HU 1987-4965	19871105
HU 197882	B	19890628		
US 4851420	A	19890725	US 1987-116807	19871105

PRIORITY APPLN. INFO.: DE 1986-3637829 A 19861106
OTHER SOURCE(S): CASREACT 109:92815; MARPAT 109:92815
GI



I

AB The title compds. (I; R1 = F; R2 = H, Cl) were prepared as analgesics and antipyretics (no data). 2,6-Diaminopyridine was slowly heated to melting and 4-FC6H4CH2Cl was added dropwise followed by heating at 130-150° for 4 h to give 59% 2,6-diamino-3-(4-fluorobenzyl)pyridine.

L25 ANSWER 29 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1987:50057 HCAPLUS
DOCUMENT NUMBER: 106:50057
TITLE: 2-Amino-3-nitro-6-(4-fluorobenzylamino)pyridine and 2-amino-3-carbethoxyamino-6-(4-fluorobenzylamino)pyridine
INVENTOR(S): Orth, Winfried; Engel, Juergen; **Emig, Peter**; Scheffler, Gerhard; Pohle, Hans
PATENT ASSIGNEE(S): Degussa A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3608762	A1	19861002	DE 1986-3608762	19860315
NO 8600825	A	19860924	NO 1986-825	19860305
EP 199951	A2	19861210	EP 1986-103517	19860315
EP 199951	A3	19871014		
EP 199951	B1	19910123		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 60322	E	19910215	AT 1986-103517	19860315
DK 8601268	A	19860924	DK 1986-1268	19860319
DK 162215	B	19910930		
DK 162215	C	19920316		
FI 8601183	A	19860924	FI 1986-1183	19860320
FI 84819	B	19911015		
FI 84819	C	19920127		
AU 8654997	A1	19860925	AU 1986-54997	19860321
AU 579922	B2	19881215		
ZA 8602138	A	19861126	ZA 1986-2138	19860321
BR 8601283	A	19861202	BR 1986-1283	19860321
ES 553222	A1	19870116	ES 1986-553222	19860321
DD 246761	A5	19870617	DD 1986-288169	19860321
CS 259887	B2	19881115	CS 1986-1986	19860321
PL 146631	B1	19890228	PL 1986-258543	19860321
IL 78218	A1	19891215	IL 1986-78218	19860321
CA 1273343	A1	19900828	CA 1986-504732	19860321
JP 61221172	A2	19861001	JP 1986-64292	19860324
JP 01046510	B4	19891009		
HU 40418	A2	19861228	HU 1986-1216	19860324
HU 206679	B	19921228		
US 4785110	A	19881115	US 1986-843253	19860324
PRIORITY APPLN. INFO.:			DE 1985-3510623	A1 19850323
			EP 1986-103517	A 19860315

OTHER SOURCE(S): CASREACT 106:50057
AB The title compds. (I and II resp.) were prepared Thus, 25-amino-3-nitro-6-methoxy-pyridine was condensed with 4-FC6H4CH2NH2 to give 95.2% I. I (26.2 g) was reduced with Raney-Ni in dioxane and acylated with ClCO2Et to give 19 g II.

L25 ANSWER 30 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:632448 HCAPLUS
DOCUMENT NUMBER: 105:232448
TITLE: Preparation of flupirtine gluconate salt for injection
INVENTOR(S): Hettche, Helmut; **Emig, Peter**; Engel, Juergen
PATENT ASSIGNEE(S): Degussa A.-G., Fed. Rep. Ger.
SOURCE: Ger. Offen., 15 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3416609	A1	19851107	DE 1984-3416609	19840505
EP 160865	A2	19851113	EP 1985-104746	19850419
EP 160865	A3	19860312		
EP 160865	B1	19880420		

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
AT 33638	E	19880515	AT 1985-104746		19850419
SU 1398772	A3	19880523	SU 1985-3884101		19850426
CS 248743	B2	19870212	CS 1985-3157		19850430
US 4673666	A	19870616	US 1985-729413		19850501
DK 8501987	A	19851106	DK 1985-1987		19850502
DK 157016	B	19891030			
DK 157016	C	19900326			
DD 236927	A5	19860625	DD 1985-275890		19850502
FI 8501752	A	19851106	FI 1985-1752		19850503
FI 80443	B	19900228			
FI 80443	C	19900611			
NO 8501772	A	19851106	NO 1985-1772		19850503
AU 8541943	A1	19851107	AU 1985-41943		19850503
ES 542817	A1	19851216	ES 1985-542817		19850503
ZA 8503351	A	19851224	ZA 1985-3351		19850503
HU 37758	A2	19860228	HU 1985-1691		19850503
HU 193753	B	19871130			
IL 75086	A1	19880331	IL 1985-75086		19850503
CA 1263398	A1	19891128	CA 1985-480723		19850503
JP 60239469	A2	19851128	JP 1985-95714		19850507
JP 01044185	B4	19890926			
PRIORITY APPLN. INFO.:			DE 1984-3416609	A	19840505
			EP 1985-104746	A	19850419

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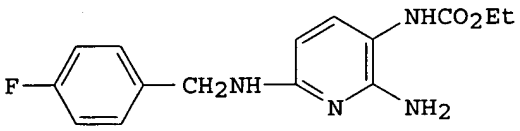

I

AB Flupirtine (I) gluconate salt is prepared by reacting I with gluconic acid or gluconic acid-δ-lactone to improve its solubility and stability. A parenteral solution can be formulated using solvents such as polyethylene glycol, glycofurol, and water. Thus I was added to a solution of gluconic acid obtained by hydrolysis of gluconic acid-δ-lactone. A mixture containing I gluconate salt, PEG, and NaHSO3 was microfiltered and stored in colorless ampules.

L25 ANSWER 31 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1984:610967 HCAPLUS
DOCUMENT NUMBER:	101:210967
TITLE:	Ethylenediamine and guanidine derivatives
INVENTOR(S):	**Emig, Peter**; Scheffler, Gerhard; Thiemer, Klaus; Weischer, Carl Heinrich
PATENT ASSIGNEE(S):	Degussa A.-G., Fed. Rep. Ger.
SOURCE:	Ger. Offen., 64 pp. CODEN: GWXXBX
DOCUMENT TYPE:	Patent
LANGUAGE:	German
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3343884	A1	19840614	DE 1983-3343884	19831205

DE 3343884	C2	19910711		
NL 8303965	A	19840702	NL 1983-3965	19831117
SU 1222196	A3	19860330	SU 1983-3663583	19831121
FR 2537582	A1	19840615	FR 1983-19390	19831205
FR 2537582	B1	19861205		
BE 898403	A1	19840606	BE 1983-47911	19831206
AU 8322138	A1	19840614	AU 1983-22138	19831206
AU 564254	B2	19870806		
GB 2132615	A1	19840711	GB 1983-32433	19831206
GB 2132615	B2	19860702		
DD 216013	A5	19841128	DD 1983-257557	19831206
DK 8305633	A	19840609	DK 1983-5633	19831207
DK 163732	B	19920330		
DK 163732	C	19920831		
FI 8304481	A	19840609	FI 1983-4481	19831207
SE 8306764	A	19840609	SE 1983-6764	19831207
ZA 8309107	A	19840725	ZA 1983-9107	19831207
ES 527864	A1	19840801	ES 1983-527864	19831207
HU 35255	O	19850628	HU 1983-4192	19831207
IL 70401	A1	19871030	IL 1983-70401	19831207
US 4738983	A	19880419	US 1983-558984	19831207
CA 1257867	A1	19890725	CA 1983-442695	19831207
AT 8304278	A	19900115	AT 1983-4278	19831207
AT 390952	B	19900725		
JP 59112980	A2	19840629	JP 1983-230710	19831208
JP 05072386	B4	19931012		
CS 241141	B2	19860313	CS 1983-9224	19831208
CH 657850	A	19860930	CH 1983-6576	19831208

PRIORITY APPLN. INFO.: DE 1982-3245387 A1 19821208

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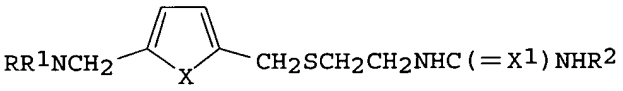

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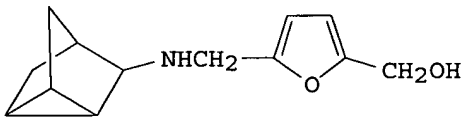
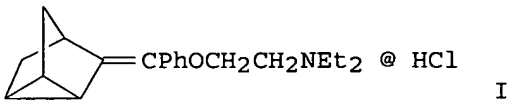


II

AB The title compds. [I; R = polycycloalkyl, (un)substituted alkyl, cycloalkyl; R1 = H, (un)substituted alkyl; R2 = H, alkenyl, alkynyl, cycloalkyl, 2-[[[5-[(dimethylamino)methyl]-2-furanyl]methyl]thio]ethyl, (un)substituted alkyl; X = O, S; X1 = R3CH, RN; R3 = NO2, cyano] were prepared Thus, 2-furanmethanol was aminomethylated with R4NH2 (R4 = tricyclo[2.2.1.22,6]hept-3-yl] and paraformaldehyde to give II, which was condensed with HSCH2CH2NH.HCl, O2NC:C(SMe)2 and MeNH2 to give I (R = R4, R1 = H, R2 = Me, X = O, X1 = O2NCH). I are as effective as ranitidine in inhibiting stomach secretion in rats.

L25 ANSWER 32 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:143000 HCAPLUS
DOCUMENT NUMBER: 98:143000
TITLE: Synthesis and structure of new basic enol ethers

AUTHOR(S): Risch, N.; **Emig, P.**; Scheffler, G.; Pohle, H.; Henkel, G.
CORPORATE SOURCE: Forsch. Geschaeftsber. Pharma, Degussa A.-G., Frankfurt/Main, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1982), 32(11), 1409-11
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 98:143000
GI



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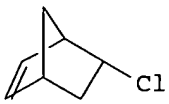

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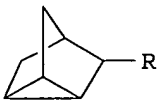

III

AB Enol ethers (E)- and (Z)-I are spasmolytics and also have antiallergy and antidepressant properties. Treating bicyclo[2.2.1]hepta-2,5-diene in CH2Cl2 with HCl(g) 6 h gave 88.2% a mixture of II and III (R = Cl). Grignard reaction of the mixture gave III [R = PhC(:NH)], hydrolysis of which gave 93.8% III (R = Bz). This, with NaNH2 and Et2NCH2CH2Cl in refluxing PhMe gave 81.7% free base, which was converted to I. X-ray anal. of (E)-I confirmed the structure.

L25 ANSWER 33 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1976:89707 HCAPLUS
DOCUMENT NUMBER: 84:89707
TITLE: Basic enol ethers and their salts
INVENTOR(S): **Emig, Peter**; Pohle, Hans; Scheffler, Gerhard; Brock, Norbert; Lenke, Hans D.; Pohl, Joerg
PATENT ASSIGNEE(S): Asta-Werke A.-G. Chemische Fabrik, Fed. Rep. Ger.
SOURCE: Ger. Offen., 35 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2413814	A1	19751002	DE 1974-2413814	19740322
DE 2413814	C3	19791004		
DE 2413814	B2	19790201		
CH 610291	A	19790412	CH 1975-2745	19750305
SE 7502607	A	19750923	SE 1975-2607	19750307
SE 421916	B	19820208		
SE 421916	C	19820527		
ZA 7501415	A	19760526	ZA 1975-1415	19750307
IL 46786	A1	19771130	IL 1975-46786	19750310
US 4065501	A	19771227	US 1975-557535	19750312
AU 7579012	A1	19760916	AU 1975-79012	19750313
GB 1446164	A	19760818	GB 1975-10992	19750317

DD 119208	C	19760412	DD 1975-184851	19750318
AT 7502073	A	19770315	AT 1975-2073	19750318
AT 339878	B	19771110		
CS 185682	P	19781031	CS 1975-1816	19750318
CS 185698	P	19781031	CS 1977-914	19750318
CA 1054152	A1	19790508	CA 1975-222446	19750318
DK 7501111	A	19750923	DK 1975-1111	19750319
DK 141818	B	19800623		
DK 141818	C	19801110		
JP 50129539	A2	19751013	JP 1975-33471	19750319
JP 58029777	B4	19830624		
FR 2264523	A1	19751017	FR 1975-8742	19750320
FR 2264523	B1	19790629		
ES 435796	A1	19761216	ES 1975-435796	19750320
PL 97364	P	19780228	PL 1975-178944	19750320
PL 97365	P	19780228	PL 1975-195370	19750320
BE 826950	A1	19750716	BE 1975-2054220	19750321
FI 7500856	A	19750923	FI 1975-856	19750321
FI 62662	B	19821029		
FI 62662	C	19830210		
NL 7503414	A	19750924	NL 1975-3414	19750321
SU 614743	D	19780705	SU 1975-2115295	19750321
HU 173792	P	19790828	HU 1975-AA807	19750321
AT 7606966	A	19770215	AT 1976-6966	19760920
AT 339278	B	19771010		
SU 639444	D	19781225	SU 1977-2440657	19770124
US 4124716	A	19781107	US 1977-842092	19771014
PRIORITY APPLN. INFO.:			DE 1974-2413814 A	19740322
			US 1975-557535 A2	19750312
			AT 1975-2073 A	19750318

GI For diagram(s), see printed CA Issue.

AB The enol ethers I (R = Ph, substituted phenyl, thienyl, pyridyl; R1 = H, Me, Et; R2 = Me, Et; NR1R2 = pyrrolidino, morpholino; n = 2,3), useful as spasmolytics were prepared Thus, II and Me2NCH2CH2Cl were added to a suspension of NaNH2 in boiling PhMe, and the mixture was refluxed for 1.5 hr to give 76% I (R = Ph, R1 = R2 = Me, n = 2). About 15 I were prepared and tested for spasmolytic activity on guinea pigs.

L25 ANSWER 34 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1970:477580 HCAPLUS

DOCUMENT NUMBER: 73:77580

TITLE: Nucleosides. X. Synthesis of dipeptidyl aminosugar nucleosides structurally related to gougerotin

AUTHOR(S): Lichtenthaler, Frieder W.; Trummlitz, G.; **Emig, Peter**

CORPORATE SOURCE: Inst. Org. Chem., Tech. Hochsch., Darmstadt, Fed. Rep. Ger.

SOURCE: Tetrahedron Letters (1970), (24), 2061-4
CODEN: TELEAY; ISSN: 0040-4039

DOCUMENT TYPE: Journal

LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB N-tert-Butoxycarbonylsarcosine, prepared from sarcosine and 2,4,5-Cl3C6H2O2COBu-tert, was treated with D-serine Me ester-HCl to give N-tert-butoxycarbonylsarcosyl-D-serine Me ester which was converted into the corresponding hydrazide. The latter treated with BuNO2 in DMF gave the corresponding azide which was coupled with 1-(3-amino-3-deoxy-β-D-glucopyranosyl)cytosine (Luebke, K., et al., 1964) to give a tert-butoxycarbonyl-blocked dipeptidyl nucleoside which on removal of the protecting group with F3CCO2H gave 1-[3-(sarcosyl-D-serylamido)-3-deoxy-

β-D-glucopyranosyl]cytosine (I). Similarly prepared was II.

L25 ANSWER 35 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:106817 HCAPLUS
DOCUMENT NUMBER: 70:106817
TITLE: Nucleosides. VIII. Configuration assignment of sugars and hexopyranosyl nucleosides by the acetyl-resonance rule
AUTHOR(S): Lichtenthaler, Frieder W.; Bambach, Gerd; **Emig, Peter**
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(3), 994-1004
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The 1H N.M.R. spectra were recorded for per-O-acetyl-D-aldopyranoses and the corresponding per-O-acetyl-2-amino-2-deoxy-D-aldopyranoses with per-O-D-gluco, D-galacto, and D-manno configurations in CDCl3 and (D3C)2SO. Results are tabulated and solvents shifts were determined Solvent shifts of the Ac protons were small (≤0.05 ppm.) in comparison with diamagnetic solvent shifts, .apprx.0.15 ppm., of the NHAc group. In fully acetylated hexopyranosyl nucleosides, the anisotropy of the base causes a general diamagnetic shift of the vicinal 2'-acetyl signals: 0.1 ppm. for pyrimidine; 0.3 ppm. for purine. Configurations of the hexopyranosyl nucleosides were thus unambiguously determined

L25 ANSWER 36 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:106813 HCAPLUS
DOCUMENT NUMBER: 70:106813
TITLE: Nucleosides. VI. Nucleoside conversion in the 3'-aminohexosyl-hypoxanthine series
AUTHOR(S): Lichtenthaler, Frieder W.; **Emig, Peter**; Bommer, Dieter
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Chemische Berichte (1969), 102(3), 971-85
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Cyclization of 2-O-[(R)-formyl(hypoxanthin-9-yl)methyl]-D-glyceraldehyde with MeNO2 yielded 9-(3-deoxy-3-nitro-β-D-glucopyranosyl)hypoxanthine and 9-(3-deoxy-3-nitro-β-D-galactopyranosyl)hypoxanthine. The latter gave upon hydrogenation 9-(3-amino-3-deoxy-β-D-galactopyranosyl)hypoxanthine. 9-(3-Acetamido-4,6-O-benzylidene - 3 - deoxy - β - D -glucopyranosyl)hypoxanthine was converted into its 2-O-(methylsulfonyl) derivative which heated with NaOAc gave 9-(3-acetamido-4,6-O-benzylidene-3-deoxy-β-D-mannopyranosyl)hypoxanthine. The latter was acetylated, after the removal of the 4,6-O-benzylidene group, to give 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-mannopyranosyl)hypoxanthine. Similarly was prepared 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-talopyranosyl)hypoxanthine, starting from 9-(3-acetamido)-4,6-O-benzylidene-3-deoxy-β-D-galactopyranosyl)hypoxanthine. Treatment of 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-glucopyranosyl)hypoxanthine with P4S10 in pyridine gave 9-(2,4,6-tri-O-acetyl-3-deoxy-3-thioacetamido-β-D-glucopyranosyl)hypoxanthine and 6-mercapto-9-(2,3,6-tri-O-acetyl-3-deoxy-3-thioacetamido-β-D-glucopyranosyl)purine (I). I was converted into the corresponding 6-(methylthio) derivative which upon ammonolysis, followed by acetylation, gave 9-(3-acetamido-2,4,6-tri-O-acetyl-3-deoxy-β-D-glucopyranosyl)adenine. The chlorination of I, followed by the addition of

Me2NH gave 9-(3-acetamido-3-deoxy-β-D-glucopyranosyl)-6-(dimethylamino)purine.

L25 ANSWER 37 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:444143 HCAPLUS
DOCUMENT NUMBER: 69:44143
TITLE: Nuclear magnetic resonance studies on sugars and cyclanols. V. Relation between the steric orientation of O- and N-acetyl groups and the methyl resonance signal location in cyclitol and aminocyclitol polyacetates
AUTHOR(S): Lichtenthaler, F. W.; **Emig, P.**
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, Fed. Rep. Ger.
SOURCE: Carbohydrate Research (1968), 7(2), 121-37
CODEN: CRBRAT; ISSN: 0008-6215
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Absorption ranges are deduced for axial and equatorial O-and N-acetyl-resonances of cyclitol and aminocyclitol peracetates on the basis of 41 ($CDCl_3$) and 22 (Me_2SO-d6) compds., allowing configurational and conformational assignments. Scope and limitations are discussed; especially application to compds. having substituents other than acetoxy and acetamido groups.

L25 ANSWER 38 OF 38 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1967:454388 HCAPLUS
DOCUMENT NUMBER: 67:54388
TITLE: N.M.R. studies on sugars and cyclanols. III. Configuration of C-methyl-branched sugars and cyclanols at the branching point
AUTHOR(S): Lichtenthaler, Frieder W.; **Emig, P.**
CORPORATE SOURCE: Tech. Hochsch., Darmstadt, Fed. Rep. Ger.
SOURCE: Tetrahedron Letters (1967), (7), 577-82
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 64: 19740c. Summary of N.M.R. studies of peracetates of sugars, cyclanols, amino sugars, and amino-cyclanols in $CDCl_3$ showed that the signal positions of acetoxy and acetamido resonances offer a convenient and generally surprisingly accurate means for configurational and conformational assignments. In view of this relationship similar relations would be expected for CMeOAc and CMeNHAc groups. In a summary of the chemical shifts in $CDCl_3$ of δ C-Me branched cyclanol acetates the differences in chemical shift between the equatorial and axial C-Me protons was small. However, the Me protons of the AcO group at the branching point showed differences of about 0.1 ppm. between axial and equatorial orientation showing the replacement of a ring H atom by a Me group causes an upward shift of the AcO signal. Accordingly, the configuration at the branching point can be deduced from the signal position of the AcO group attached to the C-Me branch of a cyclanol. A similar upward shift can be assumed for the Me protons of acetamido groups when an Me group is substituted for the ring H atom. The expected range for axial C-Me acetamido groups would thus be 8.07-8.14 τ as compared with 8.13-8.22 τ for their equatorial counterparts. Of the 7 C-Me branched aminocyclanol and amino sugar acetates which have been prepared and whose configuration at the branching point had not been assigned, the acetamido signals appear within the very small range of 0.05 ppm. and on the basis of their chemical shifts (8.15-8.20 τ) indicated an equatorial acetamido group in each compound and permitted the configurational assignments given. Since all compds. were prepared by cyclization of a

dialdehyde with EtNO2, it was concluded that the EtNO2 cyclization proceeds analogous to the MeNO2-dialdehyde cyclization, with the NO2 group preferentially, if not exclusively, attaining the equatorial position in the cyclization step.

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L5              STR
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L27            41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L26 NOT (L20 OR L23 OR L25)


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L27  ANSWER 1 OF 41  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:544300  HCAPLUS
DOCUMENT NUMBER:          143:146816
TITLE:                    Antagonist and agonist binding models of the human
                          gonadotropin-releasing hormone receptor
AUTHOR(S):                Soederhaell, J. Arvid; Polymeropoulos, Emmanuel
                          E.; Paulini, Klaus; Guenther, Eckhard; Kuehne,
                          Ronald
CORPORATE SOURCE:         Institute for Molecular Pharmacology, Berlin, D-13125,
                          Germany
SOURCE:                   Biochemical and Biophysical Research Communications
                          (2005), 333(2), 568-582
                          CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER:                Elsevier
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

AB G-protein-coupled receptors (GPCRs) constitute one of the most important classes of drug targets. Since the first high-resolution structure of a GPCR was determined by K. Palczewski and co-workers (2000), development of in silico models of rhodopsin-like GPCRs could be rationally founded. In this work, we present a model of the human gonadotropin-releasing hormone receptor based on the rhodopsin structure. The transmembrane helixes are modeled by homol., while the extra- and intracellular loops are modeled in such a way that exptl. determined interactions and microdomains (e.g., hydrophobic cores) are retained. We conclude that specifically tailored models, compared to more automatic approaches, have the benefit that known

interactions are easily introduced early in the homol. modeling. Furthermore, tailored models, although more tedious to construct, are better suited for drug lead finding and for compound optimization. To test the stability of the receptor, we performed a 1 ns mol. dynamics simulation. Moreover, we docked two agonists (native GnRH and Triptorelin) and two antagonists (Cetrorelix and the covalently constrained dicyclic decapeptide dicyclo(1,1'-5/4-10)[Ac-Glu1(Gly1')-DCpa2-DTrp3-Asp4-Dbu5-DNal6-Leu7-Arg8-Pro9-Dpr10-NH2]) into the putative receptor binding site. The docked ligand conformations result in ligand-receptor interactions that are generally in good agreement with site-directed mutagenesis and ligand-binding studies presented in the literature. Our results indicate that the binding conformation of the antagonists differs from that of the agonists. This difference can be linked to the activation or inhibition of the receptor.

REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 2 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:658086 HCAPLUS
DOCUMENT NUMBER: 137:185497
TITLE: Preparation of quinolines, isoquinolines and phthalazines as GnRH antagonists
INVENTOR(S): Strehlke, Peter; Droescher, Peter; Buehmann, Ulrich; Schmees, Norbert; Muhn, Peter; Hess-Stumpp, Holger; Kuehne, Roland; Guenther, Eckhard; **Polymeropoulos, Emmanuel**; Ter Laak, Antonius Marinus
PATENT ASSIGNEE(S): Schering Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002066437	A1	20020829	WO 2002-EP1882	20020221
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10108271	A1	20020822	DE 2001-10108271	20010221
CA 2438709	AA	20020829	CA 2002-2438709	20020221
EP 1362034	A1	20031119	EP 2002-716803	20020221
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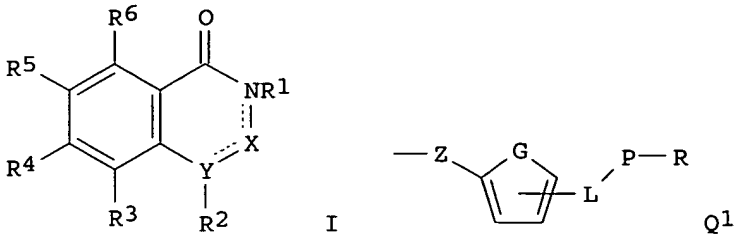
BR 2002007451	A	20040601	BR 2002-7451	20020221
JP 2004528298	T2	20040916	JP 2002-565954	20020221
NZ 527597	A	20041029	NZ 2002-527597	20020221
NO 2003003698	A	20031020	NO 2003-3698	20030820
BG 108165	A	20040831	BG 2003-108165	20030909

PRIORITY APPLN. INFO.:			
DE 2001-10108271	A	20010221	
US 2001-274914P	P	20010313	
WO 2002-EP1882	W	20020221	

OTHER SOURCE(S): MARPAT 137:185497
GI



AB Title compds. [I; R1 = COR11, cyano, CO2R12, CONR12R13, etc.; R11, R12 = (saturated) (hetero)cyclyl, alkyl, (substituted) Ph, furanyl, thiophenyl; R13 = H, alkyl; R2 = CHR21R22, etc.; R21 = H, alkyl, (substituted) Ph; R22 = (substituted) Ph, naphthyl; R3 = H, alkyl; R4 = H, alkyl, halo; R5 = Q1; G = CH:CH, CH:N, N:CH, O, S; Z = bond, O, S, etc.; L = CH2, NH; P = CO, SOx; x = 0-2; R = (substituted) amino, (branched) (substituted) alkyl, 3-7 membered cycloalkyl; R6 = CH2NR61R62; R61 = H, alkyl; R62 = alkyl, (substituted) aralkyl], were prepared Thus, a mixture of N-benzylamine and N,N-diisopropylethylamine was added to 78 mg 6-(4-acetamidophenoxy)-5-(chloromethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid Et ester (preparation given) in DMF at 0° followed by stirring for 20 h at room temperature to give 70 mg 6-(4-acetamidophenoxy)-5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester. The anal. of the antagonistic activity is given.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 3 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:632477 HCAPLUS
DOCUMENT NUMBER: 137:154937
TITLE: Preparation of quinolines, isoquinolines and phthalazines as GnRH antagonists
INVENTOR(S): Strehlke, Peter; Droescher, Peter; Buehmann, Ulrich; Schmees, Norbert; Muhn, Peter; Hess-Stumpp, Holger; Kuehne, Roland; Guenther, Eckhard; **Polymeropoulos, Emmanuel**; Ter Laak, Antonius Marinus
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: Ger. Offen., 18 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10108271	A1	20020822	DE 2001-10108271	20010221
CA 2438709	AA	20020829	CA 2002-2438709	20020221
WO 2002066437	A1	20020829	WO 2002-EP1882	20020221

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PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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US 2003105328	A1	20030605	US 2002-78530		20020221
US 6790858	B2	20040914			
EP 1362034	A1	20031119	EP 2002-716803		20020221
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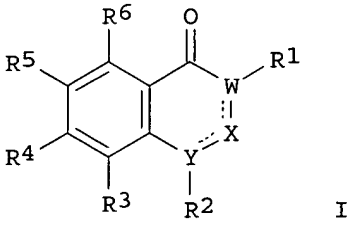
CN 1496354	A	20040512	CN 2002-806359		20020221
BR 2002007451	A	20040601	BR 2002-7451		20020221
JP 2004528298	T2	20040916	JP 2002-565954		20020221
NZ 527597	A	20041029	NZ 2002-527597		20020221
ZA 2003006429	A	20040211	ZA 2003-6429		20030819
NO 2003003698	A	20031020	NO 2003-3698		20030820
BG 108165	A	20040831	BG 2003-108165		20030909
US 2005004127	A1	20050106	US 2004-896961		20040723
PRIORITY APPLN. INFO.:			DE 2001-10108271	A	20010221
			US 2001-274914P	P	20010313
			US 2002-78530	A3	20020221
			WO 2002-EP1882	W	20020221

OTHER SOURCE(S): MARPAT 137:154937
GI



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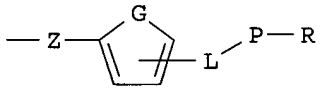

Q1

AB Title compds. [I; R1 = COR11, cyano, CO2R12, CONR12R13, etc.; R11, R12 = (saturated) cyclyl, heterocyclyl, alkyl, (substituted) Ph, furanyl, thiophenyl; R13 = H, alkyl; R2 = CHR21R22, etc.; R21 = H, alkyl, (substituted) Ph; R22 = (substituted) Ph, naphthyl; R3 = H, alkyl; R4 = H, alkyl, halo; R5 = Q1; G = C:C, C:N, N:C, O, S; Z = bond, O, S, etc.; L = CH2, NH; P = CO, SOx; x = 0-2; R = (substituted) amino, (branched) alkyl, 3-7 membered cycloalkyl; R6 = CH2NR61R62; R61 = H, alkyl; R62 = alkyl, (substituted) aralkyl, heteroarylalkyl, etc.], were prepared Thus, N-benzylamine and N,N-diisopropylethylamine was added to 78 mg 6-(4-acetamidophenoxy)-5-(chloromethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester (preparation given) in DMF at 0° followed by stirring for 20 h at room temperature to give 70 mg 6-(4-acetamidophenoxy)-5-(N-benzyl-N-methylaminomethyl)-1-(2,6-difluorobenzyl)-1,4-dihydro-4-oxoquinoline-3-carboxylic acid Et ester. The anal. of the antagonistic activity is given.

L27 ANSWER 4 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:332190 HCAPLUS
DOCUMENT NUMBER: 136:340669

TITLE: Novel 7-azaindolecarboxamides as phosphodiesterase 4 inhibitors

INVENTOR(S): Hoefgen, Norbert; Egerland, Ute; Kronbach, Thomas; Marx, Degenhard; Szelenyi, Stefan; Kuss, Hildegard; **Polymeropoulos, Emmanuel**

PATENT ASSIGNEE(S): Arzneimittelwerk Dresden Gmbh, Germany

SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034747	A1	20020502	WO 2001-EP12376	20011025
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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DE 10053275	A1	20020502	DE 2000-10053275	20001027
CA 2428468	AA	20020502	CA 2001-2428468	20011025
AU 2002021753	A5	20020506	AU 2002-21753	20011025
EP 1330455	A1	20030730	EP 2001-988718	20011025
EP 1330455	B1	20050803		
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EE 200300166	A	20030815	EE 2003-166	20011025
BR 2001014903	A	20031014	BR 2001-14903	20011025
JP 2004512337	T2	20040422	JP 2002-537738	20011025
NZ 525369	A	20040924	NZ 2001-525369	20011025
NO 2003001722	A	20030414	NO 2003-1722	20030414
BG 107725	A	20040831	BG 2003-107725	20030416
ZA 2003003236	A	20030731	ZA 2003-3236	20030425
HR 2003000427	A1	20030831	HR 2003-427	20030526
US 2004106641	A1	20040603	US 2003-399051	20030617

PRIORITY APPLN. INFO.:

DE 2000-10053275	A	20001027
US 2000-244342P	P	20001030
WO 2001-EP12376	W	20011025

OTHER SOURCE(S): CASREACT 136:340669; MARPAT 136:340669

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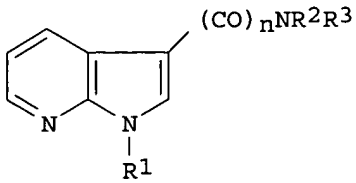


I

AB 7-Azaindoles I [n = 1, 2; R1 = (un)substituted alkyl, alkenyl; R2, R3 = H, (un)substituted alkyl, Ph, pyridyl, uracilyl, triazolyl; NR2R3 =

morpholino, thiomorpholino, thiomorpholine S,S-dioxide, 4-methylpiperazino] were prepared for use as PDE-4 inhibitors. Thus, 1-cyclopropylmethyl-7-azaindole-3-carboxylic acid was converted to the acid chloride and treated with 4-aminomethylpyridine to give the amide which had an IC50 for PDE-4 inhibition of 0.710 μmol./L.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 5 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:883024 HCAPLUS
DOCUMENT NUMBER: 134:126130
TITLE: Molecular dynamics simulations of the binding of a GnRH agonist to a model GnRH receptor
AUTHOR(S): ter Laak, A. M.; Kuhne, R.; Krause, G.; **Polymeropoulos, E. E.**; Kutscher, B.; Gunther, E.
CORPORATE SOURCE: Forschungsinstitut fur Molekulare Pharmakologie, Berlin, 10315, Germany
SOURCE: Molecular Modeling and Prediction of Bioactivity, [Proceedings of the European Symposium on Quantitative Structure-Activity Relationships: Molecular Modeling and Prediction of Bioactivity], 12th, Copenhagen, Denmark, Aug. 23-28, 1998 (2000), Meeting Date 1998, 397-398. Editor(s): Gundertofte, Klaus; Jorgensen, Flemming Steen. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69ASO3
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Gonadotropin-releasing hormone (GnRH) is the naturally occurring agonist for the G-protein-coupled GnRH receptor. GnRH stimulates the pituitary gland to produce LH and FSH, and both GnRH agonists and antagonists are potentially useful in the treatment of hormone dependent ailments. The aim of the present modeling study is the generation of a 3D-model for the binding of GnRH agonists to the GnRH receptor model using a mol. dynamics protocol with carefully designed range distance restraint functions. At a second stage in the same mol. dynamics run, the possible conformational changes within the receptor after agonist binding are investigated by simulating hypothetical conformational changes of selected conserved amino acid side chains within the GnRH receptor.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 6 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:883023 HCAPLUS
DOCUMENT NUMBER: 134:360953
TITLE: A peptidic binding site model for PDE 4 inhibitors
AUTHOR(S): **Polymeropoulos, E. E.**; Hofgen, N.
CORPORATE SOURCE: Corporate R&D, ASTA Medica Group, Department of Chemical Research, Frankfurt, D-60314, Germany
SOURCE: Molecular Modeling and Prediction of Bioactivity, [Proceedings of the European Symposium on Quantitative Structure-Activity Relationships: Molecular Modeling and Prediction of Bioactivity], 12th, Copenhagen, Denmark, Aug. 23-28, 1998 (2000), Meeting Date 1998, 395-396. Editor(s): Gundertofte, Klaus; Jorgensen, Flemming Steen. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69ASO3
DOCUMENT TYPE: Conference

LANGUAGE: English
AB Selective inhibitors of the isoenzyme phosphodiesterase 4 (PDE 4) have attracted increased interest as potential drugs for the treatment of allergic diseases such as asthma. The pharmacophore requirements for inhibiting catalytic activity have been recently analyzed. To further refine this pharmacophore model and define a peptidic model for PDE 4 inhibitors that has the ability to semi-qual. predict inhibitory activity, the program PrGen has been used.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 7 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:567784 HCAPLUS
DOCUMENT NUMBER: 133:272153
TITLE: Langmuir Monolayers with Fluorinated Groups in the Hydrophilic Head. 1. Comparison of Trifluoroethyl Behenate and Ethyl Behenate Monolayers: Molecular Models, Mechanical Properties, Stability
AUTHOR(S): Petrov, J. G.; **Polymeropoulos, E. E.**; Moehwald, H.
CORPORATE SOURCE: Max-Planck Institute of Colloids and Interfaces, Golm/Potsdam, D-14476, Germany
SOURCE: Langmuir (2000), 16(19), 7411-7420
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In a series of three related papers we compare mech. properties and stability, morphol. and structure, and electrostatic potential and ellipsometric thickness of trifluoroethyl behenate (TFEB) and Et behenate (EB) Langmuir monolayers. The aim of these papers is to study the effect of fluorination of a Me group in the hydrophilic head on monolayer properties and structure. In the present Part 1 we show that trifluoroethyl ester forms significantly more unstable films with higher compressibility (lower compressional modulus) than the unsubstituted Et ester. Both TFEB and EB surface pressure-area isotherms show compression-expansion hysteresis, but this hysteresis is larger for the fluorinated ester. The surface pressure-area loop of TFEB is shifted to larger mol. areas as compared to EB and gives larger limiting mol. areas at zero compression. This points to different vols. and/or conformations of the fluorinated and nonsubstituted hydrophilic heads. Maps of mol. lipophilicity and mol. electrostatic potential, based on semiempirical quantum mech. models of the two mols. in vacuo, relate the observed differences in monolayer properties to decreased hydrophilicity of the trifluoroethyl group and a stronger electrostatic repulsion between the hydrocarbon chains of TFEB. Such a repulsion results from polarization of the CH2 groups adjacent to the heads that is more significant for the trifluoroethyl behenate mol.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 8 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:55462 HCAPLUS
DOCUMENT NUMBER: 132:202635
TITLE: A peptidic binding site model for PDE 4 inhibitors
AUTHOR(S): **Polymeropoulos, Emmanuel E.**; Hofgen, Norbert
CORPORATE SOURCE: Department of Chemical Research, Corporate R and D ASTA Medica Group, Frankfurt, D-60314, Germany
SOURCE: Quantitative Structure-Activity Relationships (1999), 18(6), 543-547

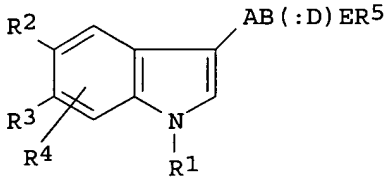
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pseudoreceptor modeling program PrGen was used to construct a peptidic binding site model for phosphodiesterase 4 inhibitors. A training set of 21 diverse compds. (rolipram, nitraquazone and xanthine derivs., imidazo pyrido pyrazinones and 5-oxyindoles) was used to construct the binding site surrogate consisting of five amino acid residues, a Zn+2 cofactor and an envelope of charged virtual particles. The model was validated by predicting the free energies of binding ΔGpred0 of ten ligands (rolipram, imidazo pyrido pyrazinones and 5-oxyindoles). In seven cases the prediction was satisfactory. The rms deviation [4] in ΔG0 is 0.16 and 1.82 kcal/mol-resulting in an uncertainty in IC50 (or Ki) of 1.32 and 22.81-for the training and the test set resp., while the corresponding maximal prediction errors in ΔGpred0 were 0.27 kcal/mol and 4.50 kcal/mol.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 9 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:708761 HCAPLUS
DOCUMENT NUMBER: 131:310549
TITLE: New hydroxyindoles and their use as phosphodiesterase 4 and TNFα inhibitors
INVENTOR(S): Hofgen, Norbert; Egerland, Ute; Poppe, Hildegard; Marx, Degenhard; Szelenyi, Stefan; Kronbach, Thomas; **Polymeropoulos, Emmanuel**; Heer, Sabine
PATENT ASSIGNEE(S): Arzneimittelwerk Dresden GmbH, Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955696	A1	19991104	WO 1999-EP2792	19990424
W: AU, BG, BR, BY, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19818964	A1	19991104	DE 1998-19818964	19980428
DE 19917504	A1	20001019	DE 1999-19917504	19990417
AU 9938229	A1	19991116	AU 1999-38229	19990424
AU 748403	B2	20020606		
BR 9910029	A	20001226	BR 1999-10029	19990424
TR 200003130	T2	20010122	TR 2000-200003130	19990424
EP 1076657	A1	20010221	EP 1999-920779	19990424
EP 1076657	B1	20040804		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002513017	T2	20020508	JP 2000-545856	19990424
NZ 507406	A	20021126	NZ 1999-507406	19990424
RU 2217422	C2	20031127	RU 2000-129678	19990424
AT 272631	E	20040815	AT 1999-920779	19990424
EP 1475377	A1	20041110	EP 2004-18391	19990424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY				
ES 2222706	T3	20050201	ES 1999-920779	19990424
CA 2270301	AA	19991028	CA 1999-2270301	19990428
US 6251923	B1	20010626	US 1999-300973	19990428
TW 530048	B	20030501	TW 1999-88106886	19990428
ZA 2000005540	A	20010327	ZA 2000-5540	20001010
BG 104842	A	20011031	BG 2000-104842	20001011
NO 2000005454	A	20001207	NO 2000-5454	20001027
HK 1035183	A1	20050415	HK 2001-105669	20010814
US 2002111351	A1	20020815	US 2002-80821	20020221
US 6545025	B2	20030408		
US 2002115651	A1	20020822	US 2002-81395	20020221
US 6545158	B2	20030408		
US 2002119971	A1	20020829	US 2002-81642	20020221
US 2002137745	A1	20020926	US 2002-81807	20020221
US 6602890	B2	20030805		
US 38624	E	20041012	US 2002-176435	20020919
US 2003134876	A1	20030717	US 2003-347659	20030120
US 6613794	B2	20030902		
US 2004220183	A1	20041104	US 2004-856034	20040527
PRIORITY APPLN. INFO.:			DE 1998-19818964	A 19980428
			DE 1999-19917504	A 19990417
			EP 1999-920779	A3 19990424
			WO 1999-EP2792	W 19990424
			US 1999-300973	A3 19990428
			US 2000-653685	A3 20000901
			US 2002-81642	A1 20020221
			US 2002-81807	A3 20020221

OTHER SOURCE(S): MARPAT 131:310549
GI



I

AB Hydroxyindoles I [R1, R5 = (un)substituted aliphatic, carbocyclic, heterocyclic, spirocyclic; R2, R3 = H, OH, ≥1 of them being OH; R4 = H, (un)substituted OH, SH, S(O)H, SO2H, NH2, CO2H, C(S)OH, NO2, CN, F, Cl, Br, I; A = alkylene, alkenylene, (CHOZ)m, CO, CS, C:NZ, O, S, NZ; Z = (un)substituted alkyl, alkenyl, carbocyclic, heterocyclic; B = C, S, SO; D = O, S, CH2, NZ; E = bond, (CH2)m, O, S, NZ; m = 0-3] were prepared I have IC50 for PDE IV inhibition of 1X10-9-1X10-5 and a selectivity relative to PDE's 2, 3, and 5 of 100-10,000. N-(3,5-dichloro-4-pyridyl)-2-[1-(4-fluorobenzyl)-5-methoxy-3-indolyl]-2-oxoacatamide was obtained by demethylation of the 5-methoxy compound and was reduced to the 2-hydroxyacetamide with NaBH4.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 10 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:469510 HCAPLUS
DOCUMENT NUMBER: 129:169977
TITLE: The real gordian knot. Racemic mixtures versus pure

enantiomers
AUTHOR(S): Szelenyi, I.; Geisslinger, G.; **Polymeropoulos, E.**; Paul, W.; Herbst, M.; Brune, K.
CORPORATE SOURCE: Arzneimittelwerk Dresden, Radebeul, D-01445, Germany
SOURCE: Drug News & Perspectives (1998), 11(3), 139-160
CODEN: DNPEED; ISSN: 0214-0934
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 225 refs. is given on racemic mixts. and enantiomers of drugs. There are often pharmacodynamic, pharmacokinetic, and/or toxicol. differences between enantiomers. The choice between developing a racemate or single enantiomers depends on therapeutic advances and developmental costs involved. Regarding the target environment for drug intervention, even if natural physiol. mediators are achiral, their receptors may demonstrate a preference for the (-)- or (+)-enantiomer of agonists or antagonists. It is also obvious that the majority of enzymes and channels are stereospecific, at least to a variable extent. From a pharmacokinetics point of view, chirality can have an influence on drug absorption, distribution, metabolism, and elimination. With a few exceptions, toxicol. differences between isomers of known drugs are less dramatic than thought to be and only seldom substantiate the necessity of a racemic switch. The pharmaceutical industry is currently very interested in the so-called "racemic switch.". Before proceeding to a racemic switch it is necessary to determine if (1) it is chemical feasible to produce a single enantiomer, (2) a clin. advantage is obtainable through a racemic switch, and (3) a marketing advantage is obtainable. The real goal of a racemic switch should be the rational development of compds. that are profitable for the company and beneficial for the patient.
REFERENCE COUNT: 225 THERE ARE 225 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 11 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:744797 HCAPLUS
DOCUMENT NUMBER: 128:30427
TITLE: Chemistry and molecular biology in the search for new LHRH antagonists
AUTHOR(S): Kutscher, Bernhard; Bernd, Michael; Beckers, Thomas; **Polymeropoulos, Emmanuel E.**; Engel, Jurgen
CORPORATE SOURCE: ASTA Med. AG, Konzernforsch., Frankfurt, D-60315, Germany
SOURCE: Angewandte Chemie, International Edition in English (1997), 36(20), 2149-2161
CODEN: ACIEAY; ISSN: 0570-0833
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 137 refs., discussing LHRH peptides as therapeutic agonists and antagonists of tumor growth, their structure and conformation, LHRH receptor assays, comparison of clin. relevant antagonists, LHRH receptor modeling, and the search for peptidomimetics for the LHRH receptor.
REFERENCE COUNT: 156 THERE ARE 156 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 12 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:549055 HCAPLUS
DOCUMENT NUMBER: 127:229228
TITLE: A pharmacophore model for PDE IV inhibitors

AUTHOR(S): **Polymeropoulos, Emmanuel E.**; Hofgen, Norbert
CORPORATE SOURCE: ASTA Medica Group, Department Chemical Research, Frankfurt/Main, D-60314, Germany
SOURCE: Quantitative Structure-Activity Relationships (1997), 16(3), 231-234
CODEN: QSARDI; ISSN: 0931-8771
PUBLISHER: Wiley-VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Based on conformational anal. and GRID-contour calcns. we developed a common primary pharmacophore for rolipram analog, nitraquazone and xanthine derivative PDE IV inhibitors. In spite of the structural differences exhibited by the three substance classes we could provide evidence that they share common hydrogen bonding and lipophilic enzyme binding sites.

L27 ANSWER 13 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:374503 HCAPLUS
DOCUMENT NUMBER: 125:104861
TITLE: D-23129: A new anticonvulsant with a broad spectrum activity in animal models of epileptic seizures
AUTHOR(S): Rostock, Angelika; Tober, Christine; Rundfeldt, Chris; Bartsch, Reni; Engel, Juergen; **Polymeropoulos, Emanuele E.**; Kutscher, Bernhard; Loescher, Wolfgang; Hoenack, Dagmar; et al.
CORPORATE SOURCE: ASTA Medica Group, Department Pharmacology, Radebeul, D-01445, Germany
SOURCE: Epilepsy Research (1996), 23(3), 211-223
CODEN: EPIRE8; ISSN: 0920-1211
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The anticonvulsant activity of the novel drug D-23129 (N-(2-amino-4-(4-fluorobenzylamino)phenyl)carbamic acid Et ester) was evaluated in animal models of epileptic seizures. D-23129 was active after oral and i.p. administration in rats and mice in a range of anticonvulsant tests at nontoxic doses. The compound was active against elec. induced seizures (MES, ED50 rat p.o. = 2.87 mg/kg), against seizures induced chemical by pentylenetetrazole (s.c. PTZ, ED50 mouse p.o. = 13.5 mg/kg), picrotoxin and N-methyl-D-aspartate (NMDA) and in a genetic animal model, the DBA/2 mouse. It was not active against seizures induced by bicuculline and strychnine. Motor impairment, evaluated with the rotarod test and by observation in the open field, was minimal at doses showing anticonvulsant activity. D-23129 was very effective in elevating the threshold for elec. and chemical induced seizures. Considering the dose increasing the MES threshold by 50% (TID50 mouse i.p. = 1.6 mg/kg; TID50 rat i.p. = 0.72 mg/kg) and the TD50 obtained in the rotarod test, the protective index of D-23129 is better than that of valproate and phenytoin. During 14 days chronic oral treatment with 15 mg/kg, no development of tolerance was observed D-23129 thus presents an orally active, safe, broad spectrum anticonvulsant agent, which is structurally unrelated to anticonvulsants currently used. We expect that D-23129 will improve the treatment of refractory seizures in humans.

L27 ANSWER 14 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:915127 HCAPLUS
DOCUMENT NUMBER: 123:305992
TITLE: Comparative Evaluation of the Predictive Power of Calculation Procedures for Molecular Lipophilicity
AUTHOR(S): Mannhold, Raimund; Rekker, Roelof F.; Sonntag, Christoph; Ter Laak, Anton M.; Dross, Karl;

Polymeropoulos, Emmanuel E.
CORPORATE SOURCE: Department of Lasermedicine, Heinrich-Heine-Universitaet, Duesseldorf, 40225, Germany
SOURCE: Journal of Pharmaceutical Sciences (1995), 84(12), 1410-19
CODEN: JPMSAE; ISSN: 0022-3549
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The predictive power of four calcn. procedures for mol. lipophilicity is checked by comparing with exptl. data (log P and chromatog. RMw) taken from the literature. Two sets of test compds. are used: the first comprises simple organic mols. and the second consists of more complicated drug mols. Our comparative evaluation leads us to conclude that the predictive power is significantly better for not too complicated organic mols. than for drugs with complicated structural pattern. The four investigated calcn. procedures should be arranged in two groups with significantly differing predictive power: (a) Rekker and Hansch/Leo and (b) Ghose/Crippen and Suzuki/Kudo. This conclusion is based on a statistical control using log P and RMw as the independent parameters. Correlations have in common: (1) slopes in correlations with calculated data based on fragmental methods are not significantly different from 1; calcns. with data from atom-based procedures show up in most cases with slopes below 1. (2) The accompanying overall statistics underline the superiority of the fragmental methods. We think that all four tested calcn. procedures have their own restrictions; for future development we would advise a thorough reconsideration of structural effects not fully (or even not at all) incorporated in the data sets. Special attention will have to be paid to the conformational aspects of lipophilic behavior.

L27 ANSWER 15 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:663436 HCAPLUS
DOCUMENT NUMBER: 121:263436
TITLE: Chemical and Biological Evaluation of Hydrolysis Products of Cyclophosphamide
AUTHOR(S): Gilard, Veronique; Martino, Robert; Malet-Martino, Marie-C.; Kutscher, Bernhard; Mueller, Arndt; Niemeyer, Ulf; Pohl, Joerg; **Polymeropoulos, Emmanuel E.**
CORPORATE SOURCE: IMRCP Laboratory, Universite Paul Sabatier, Toulouse, 31062, Fr.
SOURCE: Journal of Medicinal Chemistry (1994), 37(23), 3986-93
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 31P NMR spectroscopy was used to study the products of the decomposition of cyclophosphamide (I) in buffered solns. at pH's ranging between 1.2 and 8.6 at 20° and at pH 7.4 at 37°. At pH 1.2, I undergoes a rapid breakdown (t1/2 = 1.4 days) of the 2 P-N bonds, giving [HN(CH2CH2Cl)2] and [H2N(CH2)3OP(O)(OH)2] as their hydrochlorides. No intermediates were detected. At pH's between 5.4 and 8.6, hydrolysis of I during 17 days led to the sole and previously unknown 9-membered ring compound (II). II resulted from the intramol. alkylation of I giving a bicyclic compound followed by the exothermal cleavage of the P-N bond in the 6-membered ring. At pH values ranging from 3.4 to 8.6, there is little degradation of I since more than 95% of initial I was still present after 7 days at 20°. Under physiol. conditions (pH 7.4, 37°) after 6 days, 45% of I was hydrolyzed (t1/2 = 6.6 days), leading essentially (30% of initial I) to II. The rate of hydrolysis of II and the nature of its hydrolysis products depended on pH over the range 0-8.6. After a

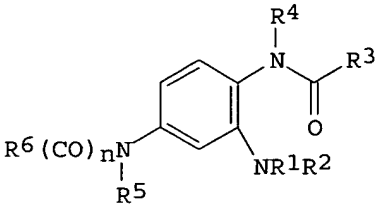
single i.p. injection to mice, II, [H2N(CH2)3OP(O)(OH)2], and [Cl(CH2)2NH(CH2)2NH(CH2)3OP(O)(OH)2] were less toxic than I. They did not exhibit any direct cytotoxic efficacy on the colony-forming capacity of L1210 cells in vitro, and they had no antitumor activity in vivo against P388 leukemia.

L27 ANSWER 16 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:569732 HCAPLUS
DOCUMENT NUMBER: 121:169732
TITLE: GABAergic activity of triamino-pyridines and triamino-benzenes
AUTHOR(S): **Polymeropoulos, E. E.**; Kutscher, B.
CORPORATE SOURCE: ASTA Med. AG, Frankfurt, 6000, Germany
SOURCE: Trends QSAR Mol. Modell. 92, Proc. Eur. Symp. Struct.-Act. Relat.: QSAR Mol. Modell., 9th (1993), Meeting Date 1992, 456-60. Editor(s): Wermuth, Camille-Georges. ESCOM: Leiden, Neth.
CODEN: 59XTAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Electron d. distribution, isopotential surfaces, and mol. electrostatic potentials were determined for GABA agonists and antagonists. The program GRID was used to evaluate non-covalent drug-receptor interactions. Conformational anal. and structure optimization were also performed.

L27 ANSWER 17 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:625705 HCAPLUS
DOCUMENT NUMBER: 119:225705
TITLE: 1,2,4-triaminobenzene derivatives and a process for their preparation
INVENTOR(S): Dieter, Hans Reinhold; Engel, Juergen; Kutscher, Bernhard; **Polymeropoulos, Emmanuel**; Szelenyi, Stefan; Nickel, Bernd
PATENT ASSIGNEE(S): Asta Medica AG, Germany
SOURCE: Ger. Offen., 11 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4200259	A1	19930715	DE 1992-4200259	19920108
EP 554543	A2	19930811	EP 1992-121028	19921210
EP 554543	A3	19931027		
EP 554543	B1	19960228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AT 134611	E	19960315	AT 1992-121028	19921210
ES 2084914	T3	19960516	ES 1992-121028	19921210
CA 2086654	AA	19930709	CA 1993-2086654	19930104
CA 2086654	C	20030923		
ZA 9300011	A	19930805	ZA 1993-11	19930104
JP 05345752	A2	19931227	JP 1993-1054	19930107
JP 3145220	B2	20010312		
US 5384330	A	19950124	US 1993-2458	19930108

PRIORITY APPLN. INFO.: DE 1992-4200259 A 19920108
OTHER SOURCE(S): CASREACT 119:225705; MARPAT 119:225705
GI



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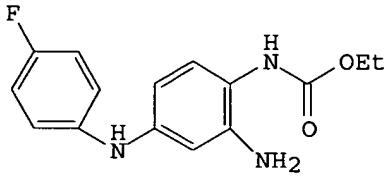

II

AB The title compds., 2-amino-1,4-bis(acylamino)benzene derivs. I (R1 = hydrogen, alkyl, etc.; R3 = alkoxy, amino, etc.; R4, R5 = hydrogen, alkyl; R6 = arylalkyl) and pharmaceuticals containing them are claimed. I are anticonvulsants, antipyretics, antiepileptics, muscle relaxants, and peripheral analgesics. Some I were tested as antiepileptics in electroshock-induced convulsions in rats. Reductive carbamoylation of 2-amino-4-[(4-fluorobenzy)amino]-1-nitrobenzene gave 2-amino-4-[(4-fluorobenzyl)amino]-1-[(ethoxycarbonyl)amino]benzene [ethyl [2-amino-4-[[(4-fluorophenyl)methyl]amino]phenyl]carbamate] (II); II dihydrochloride was obtained in 73% yield.

L27 ANSWER 18 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:594860 HCAPLUS
DOCUMENT NUMBER: 119:194860
TITLE: l-Deprenyl: A unique MAO-B inhibitor
AUTHOR(S): **Polymeropoulos, E. E.**
CORPORATE SOURCE: Dep. Sci. Inf., ASTA Med. A.-G., Frankfurt/Main, Germany
SOURCE: Inhib. Monoamine Oxidase B (1993), 109-24. Editor(s): Szelenyi, Istvan. Birkhaeuser: Basel, Switz. CODEN: 59HWAP
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 32 refs.

L27 ANSWER 19 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:622766 HCAPLUS
DOCUMENT NUMBER: 115:222766
TITLE: Computer-assisted analysis of the possible binding sites of H1-antagonists
AUTHOR(S): **Polymeropoulos, E. E.**; Kutscher, B.; Fleischhauer, I.
CORPORATE SOURCE: ASTA Pharma A.-G., Frankfurt, D-6000/1, Germany
SOURCE: Pharmacochemistry Library (1991), 16(QSAR: Ration. Approaches Des. Bioact. Compd.), 761-4 CODEN: PHLIDQ; ISSN: 0165-7208
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of antiallergic-antihistaminic compds. acting as H1-receptor antagonists was analyzed with regard to their structural and electronic properties by means of the quantum mech. methods and the program GRID. A model defining possible common binding sites is suggested.

L27 ANSWER 20 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:227015 HCAPLUS
DOCUMENT NUMBER: 108:227015
TITLE: Structure and dynamics of noble gas clusters and cluster ions

AUTHOR(S): Brickmann, J.; **Polymeropoulos, E. E.**; Meisel, D.
CORPORATE SOURCE: Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Contrib. - Symp. At. Surf. Phys. (1986), 342-9. Editor(s): Howorka, F.; Lindinger, W.; Maerk, T. D. Inst. Atomphys. Univ. Innsbruck: Innsbruck, Austria. CODEN: 56GBA4
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 15 refs. is given of authors own and related work.

L27 ANSWER 21 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:529434 HCAPLUS
DOCUMENT NUMBER: 103:129434
TITLE: Magic numbers in ionized rare-gas clusters
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chemie, Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Surface Science (1985), 156(2), 563-71 CODEN: SUSCAS; ISSN: 0039-6028
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The relative stability of ionized rare-gas clusters Xn+, with n = 5-20 for Arn+ and n = 5-26 for Xen+ was studied by means of a combined mol. dynamics and Monte Carlo technique. Stable ionized clusters with "magic nos." n = 19 for Ar and n = 13, 19 and 25 for Xe occur, in agreement with exptl. time-of-flight mass spectra.

L27 ANSWER 22 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:518290 HCAPLUS
DOCUMENT NUMBER: 103:118290
TITLE: Molecular dynamics of ion transport through transmembrane model channels
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Annual Review of Biophysics and Biophysical Chemistry (1985), 14, 315-30 CODEN: ARBCEY; ISSN: 0883-9182
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 101 refs., of mol. dynamics of ion transport through transmembrane model channels (i.e., ionophore channels), including the use of simulation methods to describe processes involved in these systems.

L27 ANSWER 23 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:442966 HCAPLUS
DOCUMENT NUMBER: 103:42966
TITLE: The stability of rare gas clusters by ionization
AUTHOR(S): **Polymeropoulos, E. E.**; Loeffler, S.; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hoch. Darmstadt, Darmstadt, D 6100, Fed. Rep. Ger.
SOURCE: Zeitschrift fuer Naturforschung, Teil A: Physik, Physikalische Chemie, Kosmophysik (1985), 40A(5), 516-19 CODEN: ZTAKDZ; ISSN: 0340-4811
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Computer simulations were made of the dissociation dynamics of Ar and Xe neutral and singly-charged clusters with 5-20 atoms. The stability of clusters with magic nos. (P. and B., 1983) of atoms (n = 19 for Ar, and n = 13, 19 for Xe), as found in time-of-flight mass spectra (J. Farges, et al., 1983), was greater for the ionized clusters than for the neutral clusters, indicating the importance of ionization on the cluster-size distribution found in expts.

L27 ANSWER 24 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:442961 HCAPLUS
DOCUMENT NUMBER: 103:42961
TITLE: Molecular-dynamics simulations in systems of rare gases using Axilrod-Teller and exchange three-atom interactions
AUTHOR(S): **Polymeropoulos, E. E.**; Bopp, P.; Brickmann, J.; Jansen, L.; Block, R.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1985), 31(6), 3565-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using previous results (P., et al., 1984), mol.-dynamics simulations of cluster formation in compressed Ar and Xe gases were done with a Lennard-Jones (6,12) potential, Axilrod-Teller 3-atom interactions, and exchange-type interactions. Selective stabilization of the clusters Ar19, Xe13, and Xe19 (possibly also Xe25) was established, predominantly as a result of the 3-atom exchange potential. These exchange contributions, in combination with selective stability due to cluster ionization, can explain the phenomena observed in existing time-of-flight mass-spectroscopy expts. on rare-gas-atom clusters.

L27 ANSWER 25 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:144899 HCAPLUS
DOCUMENT NUMBER: 102:144899
TITLE: Solvent effects in ionic transport through transmembrane protein channels
AUTHOR(S): Kappas, U.; Fischer, W.; **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-1600, Fed. Rep. Ger.
SOURCE: Journal of Theoretical Biology (1985), 112(3), 459-64
CODEN: JTBIAP; ISSN: 0022-5193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ion transport through a gramicidin A-like channel in the presence of solvent mols. with van der Waals parameters of H2O was studied by means of mol. dynamics simulation. The presence of solvent mols. in the channel tended to equalize the effective masses of ions through association, thus predicting the exptl. observed ion selectivity of the gramicidin A channel.

L27 ANSWER 26 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:119844 HCAPLUS
DOCUMENT NUMBER: 102:119844
TITLE: Exchange perturbation theory calculations of the interaction energy between two ground-state hydrogen atoms
AUTHOR(S): Adams, William H.; Clayton, Meredith M.; **Polymeropoulos, E. E.**

CORPORATE SOURCE: Dep. Chem., Rutgers Univ., New Brunswick, NJ, 08903, USA
SOURCE: International Journal of Quantum Chemistry, Quantum Chemistry Symposium (1984), 18, 393-406
CODEN: IJQSDI; ISSN: 0161-3642
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of calcns. were made of the interaction energy between two H atoms in their ground states, using three kinds of exchange perturbation theory. One objective was to test the accuracy that could be achieved with these perturbation methods. A second was to see if the results were consistent with those for H2+. The perturbation equations were solved within the CI approximation, using 226 partially symmetry-contracted, two-electron basis functions. The set of Slater-type basis orbitals was chosen so that we could approx. within 2% the most accurate calculated interaction energies. The second-order energies were reported at a series of nuclear separation and compare them to the best values that have been published. Some of the published values are inaccurate. The % errors in the interaction energies approximated by summing through second and third orders were given.

L27 ANSWER 27 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:577869 HCAPLUS
DOCUMENT NUMBER: 101:177869
TITLE: Analysis of three-body potentials in systems of rare-gas atoms: Axilrod-Teller versus three-atom exchange interactions
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.; Jansen, L.; Block, R.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1984), 30(4), 1593-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The triple-dipole (Axilrod-Teller) and the exchange 3-atom potentials were compared for a number of specific arrangements of 3 argon atoms and 3 xenon atoms. For these configurations, total potentials were constructed, taking a Lennard-Jones (6-12) potential for each pair. For all arrangements, the exchange 3-atom potential was the most important correction to the two-body interaction. Qual., the changes with respect to the 2-body potential were more pronounced for Xe than for Ar.

L27 ANSWER 28 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:57103 HCAPLUS
DOCUMENT NUMBER: 100:57103
TITLE: The influence of three-body forces on the lifetime and stability of rare gas clusters
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1983), 87(12), 1190-5
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters in compressed Ar and Xe gases is studied with the mol. dynamics simulation technique using 2-body Lennard-Jones and 3-body Axilrod-Teller interaction potentials. The effect of 3-body

interactions is a function of the temperature of the system and increases with decreasing temperature The occurrence of clusters corresponding to the "magic-number" n = 13 for Xe is explained in terms of the dispersion forces inherent in the Axilrod-Teller potential. Computer generated images of stable and unstable Xe13 clusters are presented.

L27 ANSWER 29 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1983:185974 HCAPLUS
DOCUMENT NUMBER: 98:185974
TITLE: On the origin of the occurrence of "magic numbers" in cluster size distributions of xenon in the compressed gas phase
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Tech. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Chemical Physics Letters (1983), 96(3), 273-5
CODEN: CHPLBC; ISSN: 0009-2614
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters in compressed Ar and Xe is studied with the mol. dynamics simulation technique using 2-body Lennard-Jones and 3-body Axilrod-Teller potentials. The occurrence of clusters corresponding to the "magic number" n = 13 for Xe and the absence of such stable clusters for Ar is due to the dispersion forces that result from triplet-dipole interaction.

L27 ANSWER 30 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1982:623356 HCAPLUS
DOCUMENT NUMBER: 97:223356
TITLE: Molecular dynamics study of the formation of argon clusters in the compressed gas
AUTHOR(S): **Polymeropoulos, E. E.**; Brickmann, J.
CORPORATE SOURCE: Inst. Phys. Chem., Techn. Hochsch. Darmstadt, Darmstadt, D-6100, Fed. Rep. Ger.
SOURCE: Chemical Physics Letters (1982), 92(1), 59-63
CODEN: CHPLBC; ISSN: 0009-2614
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The formation of clusters (nucleation) in compressed Ar gas was studied via mol.-dynamics simulation with 2-body Lennard-Jones and 3-body Axilrod-Teller potentials. The 3-body interactions become increasingly important, with decreasing temperature, for cluster stability and cluster size distributions.

L27 ANSWER 31 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1981:93471 HCAPLUS
DOCUMENT NUMBER: 94:93471
TITLE: Photoinitiated electron transfer between donors and acceptors in monomolecular layer assemblies - EPR and optical studies
AUTHOR(S): Cunningham, J.; **Polymeropoulos, E. E.**; Moebius, D.; Baer, F.
CORPORATE SOURCE: Max Planck-Inst. Biophys. Chem., Goettingen, D 3400, Fed. Rep. Ger.
SOURCE: NATO Advanced Study Institutes Series, Series C: Mathematical and Physical Sciences (1980), 61(Magn. Reson. Colloid Interface Sci.), 603-8
CODEN: NASCD6; ISSN: 0377-2071
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Studies were made by EPR and fluorescence quenching (FQ) techniques of factors influencing photoinitiated electron transfer from donor species organized as one monomol. layer towards acceptor mols. located 20 Å distant in another monomol. layer. Whenever a paraquat type acceptor was incorporated, illumination at wavelengths absorbed by different cyanine or porphyrin donors yielded a weak anisotropic EPR signal consistent with formation of appropriately aligned alkyl-viologen radicals by electron trapping. Time scale and efficiency of EPR signal growth, allied to dependence on thickness of the spacing monolayer, differed markedly from characteristics of FQ. Implications of these differences for relative rates of processes following photoinitiated charge separation in the monolayer assemblies are considered.

L27 ANSWER 32 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:642620 HCAPLUS
DOCUMENT NUMBER: 93:242620
TITLE: Monolayer assemblies with functional units of sensitizing and conducting molecular components: photovoltage, dark conduction and photoconduction in systems with aluminum and barium electrodes
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.; Kuhn, H.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, D 3400, Fed. Rep. Ger.
SOURCE: Thin Solid Films (1980), 68(1), 173-90
CODEN: THSFAP; ISSN: 0040-6090
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The vectorial change separation was studied in assemblies in which a mixed monolayer of an indocarbocyanine dye with the chromophores in the layer plane, a chain-like π electron system oriented perpendicular to the layer plane, and a layer of acceptor mols. were sandwiched between metal electrodes. The cyanine dye was excited by light, and the excited electron could move via the π electron system and the acceptor to the pos. biased electrode. If these arrangements are sandwiched between metals of very different work functions (Al and Ba), a photovoltage can be measured and is interpreted as being caused by a vectorial electron transfer through the mol. functional unit towards the metal with the smaller work function. The dark conductivity through fatty acid multilayers sandwiched between an Al and a Ba electrode was measured and was interpreted. The hopping of electrons between interlayer states adjacent to the Al electrode is rate-limiting.

L27 ANSWER 33 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:224221 HCAPLUS
DOCUMENT NUMBER: 92:224221
TITLE: Photochromism in monolayers
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, D-3400, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1979), 83(12), 1215-22
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The photochromic properties of 1'-octadecyl-3',3'-dimethyl-6-nitropiro[2H-1-benzopyran-2,2'-indoline](I) were studied in monolayers at the air-H2O interface by measuring the surface pressure-area isotherms and the surface potential of several mixts. of I with tripalmitine. By using the Langmuir-Blodgett technique, mixed monolayers of tripalmitine and I in a molar mixing ratio of 6:1 were transferred onto glass slides and their

photochromic properties in monolayer assemblies were studied.

L27 ANSWER 34 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:203868 HCAPLUS
DOCUMENT NUMBER: 92:203868
TITLE: Exchange perturbation theory. IV. Calculations on diatomic hydrogen (H) ion
AUTHOR(S): Adams, William H.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Dep. Chem., Rutgers, State Univ., New Brunswick, NJ, 08903, USA
SOURCE: Journal of Chemical Physics (1980), 72(5), 2981-9
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Authors have applied the two localized-wave-functions (LW) exchange-perturbation-theories (EPT) which they have proposed (1978) to the 1sσg and 2pσu states of H2+ with the objective of verifying the insights gained from these EPT's and testing their accuracy. The one LW EPT dets. a primitive wave function identical to that of the Eisenschitz-London EPT through first order, but which differs from it in all higher orders. The other dets. a function identical to that of the Hirschfelder-Silbey EPT through first order and through infinite order, but which differs from it through all intermediate orders. In terms of the perturbation expansion of the interaction energy through third order, authors' EPT's are as accurate as the original EPT's to which they are related. The LW EPT's have the conceptual asset that their primitive wave functions are least distorted from the zero order wave function in a precisely defined sense. Interaction energies were also calculated using the integrals which define the interaction energies in terms of LW's, and substituting the LW's approximated by sums through first, second, and third order. The energies generally increase in accuracy as the LW is summed to higher orders. When each order contribution to the LW is multiplied by a weight which is determined to minimize the interaction energy, and the LW is summed through third order, the interaction energy is in error by 0.07% or less for nuclear sepns. ranging from 1.0 to 10.0 bohr. An examination of the LW's shows how the optimization procedure works. Other quantities are calculated which show that the LW EPT's are systematically refinable methods for the calcn. of LW's as well as for the calcn. of interaction energies. This is important because LW'S may be used to calculate distinct "phys." contributions to interaction energies.

L27 ANSWER 35 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1979:131519 HCAPLUS
DOCUMENT NUMBER: 90:131519
TITLE: Electron tunneling through superconducting aluminum/monolayer/lead junctions
AUTHOR(S): **Polymeropoulos, E. E.**
CORPORATE SOURCE: Abt. Mol. Syst., Mas-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Solid State Communications (1978), 28(10), 883-5
CODEN: SSCOA4; ISSN: 0038-1098
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The current-voltage characteristics of Al/adsorbed monolayer/Pb junctions was determined at 77, 4.2, and 1.8 K for applied voltages 1-3 mV. At 77 K the current changes linearly with voltage whereas at 4.2 and 1.8 K the relation becomes nonlinear. Based on results at 1.8 K, an approx. band gap for Pb equal to 2.6 meV was obtained. The observation of a nonlinear current-voltage characteristic at temps. where Pb becomes superconducting

is strong evidence that the observed current through the insulator is a tunneling current.

L27 ANSWER 36 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:589545 HCAPLUS
DOCUMENT NUMBER: 89:189545
TITLE: Electrical conduction through adsorbed monolayers
AUTHOR(S): **Polymeropoulos, E. E.**; Sagiv, J.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Journal of Chemical Physics (1978), 69(5), 1836-47
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Elec. conduction was studied in Al/adsorbed monolayer/Al junctions. The adsorbed monolayers were long chain saturated fatty acids (23-14 C atom chain), short chain perfluorinated fatty acids (10-7 C atom chain), and n-octadecyltrichlorosilane. The current observed decreased rapidly with decreasing temperature from 295 K to .apprx.77 K at which point the decrease in current with decreasing temperature became very small. At room temperature (295 K)
there was no definite relation between the d.c. conductivity and the length of the fatty acids. At ≤77 K, however, the d.c. conductivity was exponentially dependent on the fatty-acid chain length. Thus, at ≤77 K the conduction mech. is tunneling through the monolayer. The tunneling barrier height was of the order of 2.8 and 5.2 eV for fatty acids and perfluorinated fatty acids, resp. By artificially producing mol. holes in monolayers, in the presence of such holds it was shown, the current increases by at least one order of magnitude while the effective barrier height is lowered by 10%. Differences between the present results and those previously obtained with monolayers deposited from an air-water interface (Langmuir-Blodgett monolayer) are discussed.

L27 ANSWER 37 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:569628 HCAPLUS
DOCUMENT NUMBER: 89:169628
TITLE: Adsorbed monolayers. Molecular organization and electrical properties
AUTHOR(S): Sagiv, J.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Max-Planck-Inst. Biophys. Chem., Karl-Friedrich-Bonhoeffer-Inst., Goettingen-Nikolausberg, Fed. Rep. Ger.
SOURCE: Berichte der Bunsen-Gesellschaft (1978), 82(9), 882
CODEN: BBPCAX; ISSN: 0005-9021
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adsorption was used to obtain monolayers with a controllable mol. organization. The adsorption process and structure of dye-containing monolayers were studied by spectroscopy. Adsorbed monolayers were used in study of elec. conductivity through organic films. Oleophobic monolayers of long-chain surfactants and mixed monolayers containing dyes were studied. Octadecyltrichlorosilane (OTS) was used as an adsorbate-adsorbent bonding agent. Mol-holes were produced in OTS + dye monolayers by removal of the dye. Addition of other mols. to those holes gives a type of mol. organization. Anisotropic mol. distributions were induced in monolayers by adsorption on oriented polymeric surfaces. The elec. properties (capacitance, current, tunneling, and dielec. constant) were studied of adsorbed monolayers on Al electrodes. These adsorbed monolayers included fatty acids, perfluorinated fatty acids, and OTS. Adsorbed monolayers may be used as insulators in Al/monolayer Pb superconducting tunneling

junctions.

L27 ANSWER 38 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:435174 HCAPLUS
DOCUMENT NUMBER: 89:35174
TITLE: Photoconduction in monolayer assemblies with functional units of sensitizing and conducting molecular components
AUTHOR(S): **Polymeropoulos, E. E.**; Moebius, D.; Kuhn, H.
CORPORATE SOURCE: Abt. Mol. Systemaufbau, Max-Planck-Inst. Biophys. Chem., Goettingen, Fed. Rep. Ger.
SOURCE: Journal of Chemical Physics (1978), 68(8), 3918-31
CODEN: JCPSA6; ISSN: 0021-9606
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vectorial charge separation was studied in assemblies where a mixed monolayer of a cyanine dye with the chromophores in the layer plane and a chainlike π-electron system oriented perpendicular to the layer plane are sandwiched between fatty acid monolayers and metal electrodes. The cyanine dye is excited by light, and the excited electrons move through the π-electron system which acts as the conducting element. Conduction takes place according to different mechanisms depending on the temperature In the low-temperature mode the logarithm of the photocurrent decreases linearly with (1/T)1/2, while in the high-temperature mode it decreases linearly with 1/T; in both modes the photocurrent is proportional to the light intensity and its logarithm increases linearly with the bias voltage. If the conducting π-electron system is absent, the photocurrent is about an order of magnitude smaller but again proportional to the light intensity. Its logarithm increases linearly with the square root of the bias voltage. The results in the complex assembly can be interpreted by assuming that the excited electron is transfered from the cyanine dye to the π-electron system by tunneling or by thermal activation over a barrier of 0.25 eV; from there it tunnels through the next fatty acid layer to an interface state, and then hops to the pos. biased electrode. This model can be checked by specifically altering the thickness of the tunneling barrier (by exchanging arachidic acid for fatty acids with shorter chain lengths). In the arrangement where the conducting element is absent, the results are interpreted by assuming that the excited electron either tunnels through or is thermally activated over the potential barrier of the hydrocarbon matrix (1 eV). The different voltage dependence in the two arrangements with and without the conducting π-electron system can be quant. explained as being due to the fact that the chromophore of the cyanine dye is perpendicular to the applied field, while the chain of the π-electron system is parallel to this field.

L27 ANSWER 39 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:126608 HCAPLUS
DOCUMENT NUMBER: 88:126608
TITLE: Exchange perturbation theory. III. Hirschfelder-Silbey type
AUTHOR(S): **Polymeropoulos, E. E.**; Adams, William H.
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 24-9
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An exchange perturbation theory is developed which yields in infinite order the same primitive function F that is found in infinite order with

the Hirschfelder-Silbey (HS) theory. The perturbation equations are identical to the HS equations only through first order. This is because the perturbing potential in our theory is not the bare interaction potential of the HS theory, but rather that potential screened by a nonlocal potential. The screening is the weakest that we have found in studying the equations satisfied by primitive functions, which are least distorted from products of the functions for the subsystems when the interactions have been turned off. It is argued that this HS-type theory is best used when the interactions are weak.

L27 ANSWER 40 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:126607 HCAPLUS
DOCUMENT NUMBER: 88:126607
TITLE: Exchange perturbation theory. II. Eisenschitz-London type
AUTHOR(S): **Polymeropoulos, E. E.**; Adams, William H.
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 18-23
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An exchange perturbation theory is developed which is identical through first order in the primitive function G with the Eisenschitz-London (EL) theory. In higher orders, G is different from the EL primitive function and from the primitive functions of related theories. The function G is least distorted from the zeroth-order function F0, a product of functions for the subsystems when the interactions have been set equal to zero. The potential which distorts F0 into G is more thoroughly screened than in any other theory we have examined This EL-type theory should be used when the unscreened interactions are strong.

L27 ANSWER 41 OF 41 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1978:126606 HCAPLUS
DOCUMENT NUMBER: 88:126606
TITLE: Exchange perturbation theory. I. General definitions and relations
AUTHOR(S): Adams, William H.; **Polymeropoulos, E. E.**
CORPORATE SOURCE: Sch. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SOURCE: Physical Review A: Atomic, Molecular, and Optical Physics (1978), 17(1), 11-17
CODEN: PLRAAN; ISSN: 0556-2791
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A class of primitive functions are defined which are least distorted from the unsymmetrized function F0, a product of atomic or other group functions, in the limit that the interactions between the groups have been turned off. These primitive functions have the property that at least one Schroedinger eigenfunction may be obtained from them by sym. projection. The screened potential is regarded as a perturbation and the corresponding Rayleigh-Schroedinger perturbation equations are derived. It is shown that a number of inequivalent, but equally valid energy expressions may be defined in terms of the primitive functions. Only when the primitive function is calculated exactly to infinite order will the different energy expressions all yield the same numerical value. It is suggested that this provides a check on the accuracy of approx. primitive functions.

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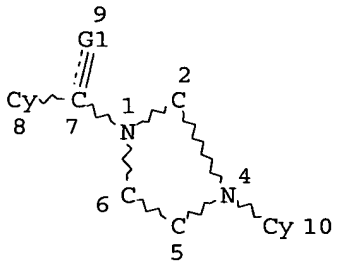

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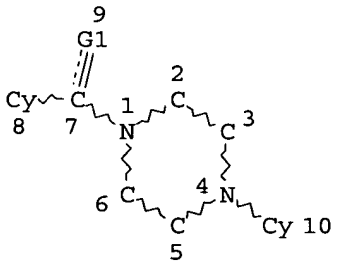

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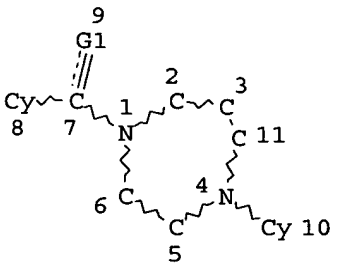

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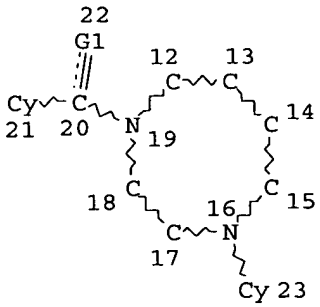
STEREO ATTRIBUTES: NONE
L11 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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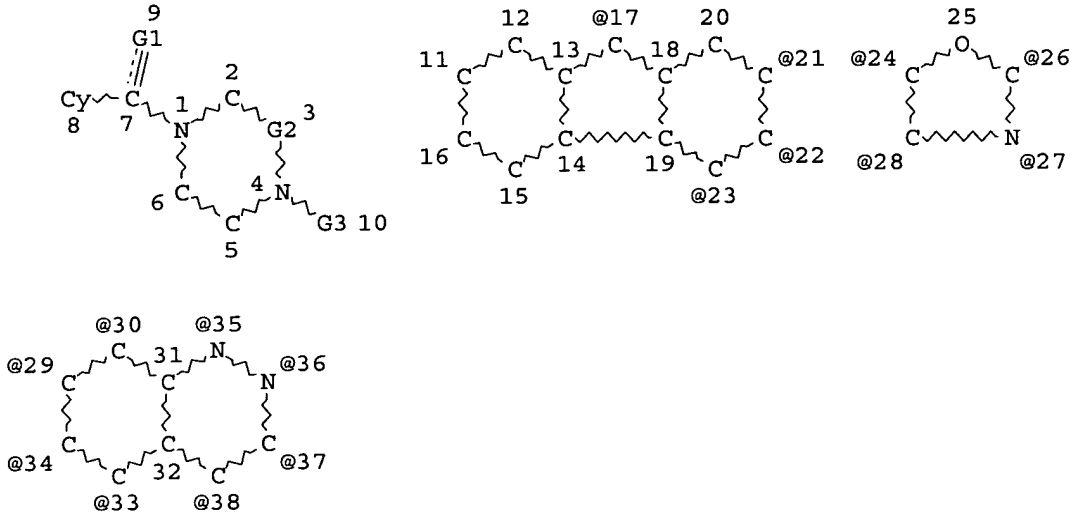
L16 STR



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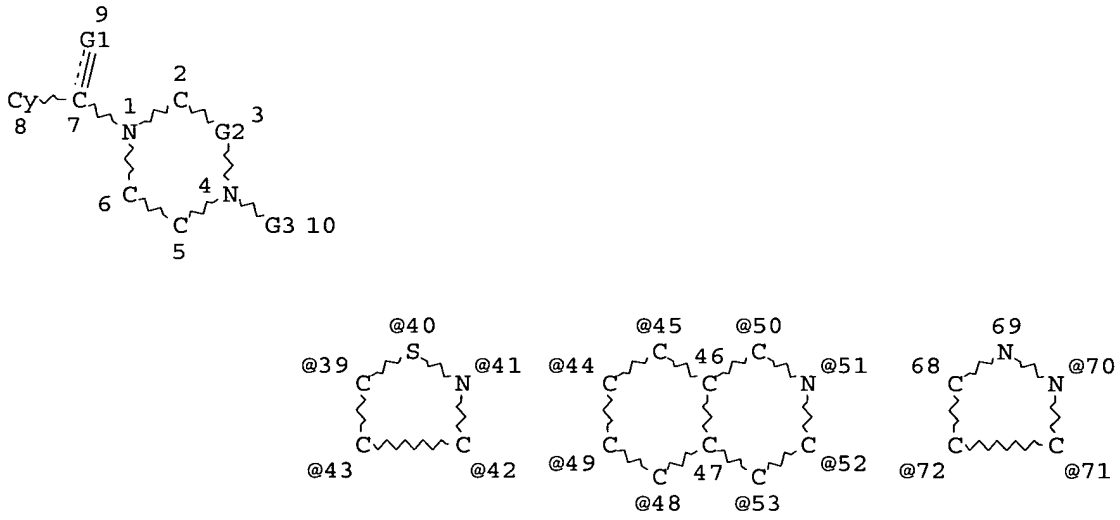
NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE
L17 STR



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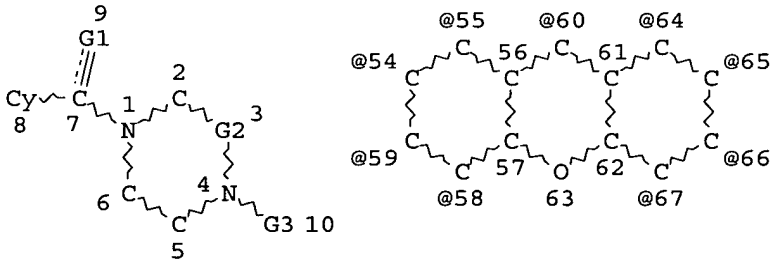
REP G2=(0-3) C
VAR G3=40/41/42/43/39/50/51/52/53/45/44/49/48/70/71/72
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 30

STEREO ATTRIBUTES: NONE
L18 STR



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REP G2=(0-3) C
VAR G3=54/55/60/64/65/66/67/58/59
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
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STEREO ATTRIBUTES: NONE
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L25          38 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L24 NOT (L20 OR L23)
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L31          11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 NOT (L20 OR L23 OR L25)


=>
=> d ibib abs l31 1-11

L31  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:252340  HCAPLUS
DOCUMENT NUMBER:          140:264487
TITLE:                    Medicaments containing disorazoles and derivatives
                          thereof for the treatment of benign and malignant
                          tumors
INVENTOR(S):              Irschik, Herbert; Jansen, Rolf; Sasse, Florenz;
                          Baasner, Silke; Schmidt, Peter; Gunther,
                          Eckhard
PATENT ASSIGNEE(S):       Zentaris GmbH, Germany
SOURCE:                   PCT Int. Appl., 30 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
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     WO 2004024149         A1    20040325    WO 2003-EP9329          20030822
         W:  AT, AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ,
             LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA
         RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
             DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
             SI, SK, TR
     CA 2438001            AA    20040224    CA 2003-2438001         20030822
     US 2004106662         A1    20040603    US 2003-646904          20030822
     EP 1536789            A1    20050608    EP 2003-794920          20030822
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, TR, BG, CZ, EE, HU, SK
     BR 2003013789         A     20050705    BR 2003-13789           20030822
PRIORITY APPLN. INFO.:                      US 2002-405594P      P  20020824
                                            WO 2003-EP9329       W  20030822
OTHER SOURCE(S):          MARPAT 140:264487
AB   The invention discloses disorazole compds. which are used as medicaments,
     preferably in the treatment of tumors, especially in the case of drug
resistance
     and in metastasizing carcinoma.  Possible uses thereof are not restricted
     to tumor diseases.
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REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:885644 HCAPLUS
DOCUMENT NUMBER: 140:26268
TITLE: Switching Off HER-2/neu in a Tetracycline-Controlled Mouse Tumor Model Leads to Apoptosis and Tumor-Size-Dependent Remission
AUTHOR(S): Schiffer, Ilka B.; Gebhard, Susanne; Heimerdinger, Carolin K.; Heling, Annette; Hast, Jochem; Wollscheid, Ursula; Seliger, Barbara; Tanner, Berno; Gilbert, Sandra; Beckers, Thomas; **Baasner, Silke**; Brenner, Walburgis; Spangenberg, Christian; Prawitt, Dirk; Trost, Tatjana; Schreiber, Wolfgang G.; Zabel, Bernhard; Thelen, Manfred; Lehr, Hans-Anton; Oesch, Franz; Hengstler, Jan G.
CORPORATE SOURCE: Departments of Radiology, Institute of Toxicology, University of Mainz, Mainz, 55131, Germany
SOURCE: Cancer Research (2003), 63(21), 7221-7231
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Overexpression of the receptor tyrosine kinase HER-2/neu is associated with poor prognosis in patients with breast and ovarian cancer. Recent excitement has surrounded the therapeutic effects of HER-2-blocking therapy strategies and has rekindled interest on the mol. mechanisms of HER-2/neu in tumor biol. To study the role of HER-2/neu overexpression in vivo, the authors used a murine fibroblast cell line (NIH3T3-her2) conditionally expressing human HER-2/neu under control of a tetracycline-responsive promoter. Expression of HER-2 could be down-regulated below detection limit (>625-fold dilution) by exposure of NIH3T3-her2 cells to anhydrotetracycline (ATc). S.c. injection of NIH3T3-her2 cells into nude mice resulted in rapid tumor growth. Mice with mean tumor vols. of 0.2, 0.8, 1.9, and 14.9 cm3 were treated daily with 10 mg/kg ATc to switch off HER-2/neu expression, producing redns. in tumor size of 100, 98.1, 81.4, and 74.2%, resp., by 7 days after onset of ATc administration. Different long-term effects of HER-2 down-regulation were observed when mice with small (0.2 cm3), intermediate (0.8-1.2 cm3) and large (≥1.9 cm3) tumors received ATc for up to 40 days. Complete remission was observed for 100, 40, and 18% of the small-, intermediate-, and large-sized tumors, resp. However, after 20-45 days of ATc administration, recurrent tumor growth was observed for all mice, even in those with previous complete remissions. The time periods for which mean tumor volume could be suppressed to vols. <0.1 cm3 under ATc administration were 34, 22, 8, and 0 days for tumors with initial vols. of 0.2, 0.8, 1.9 and 14.9 cm3, resp. Interestingly, HER-2 remained below the detection limit in recurrent tumor tissue, suggesting that initially HER-2-dependent tumors switched to HER-2 independence. The "second hits" leading to HER-2-independent tumor growth have not yet been identified. The rapid regression of tumors after down-regulation of HER-2 was explained by two independent mechanisms: (a) a block in cell cycle progression, as evidenced by a decrease in Ki-67 antigen expression from 40% before ATc treatment to 8.3% after 7 days of ATc treatment; and (b) induction of apoptosis as demonstrated by caspase-3 activation and by the terminal deoxynucleotidyltransferase (Tdt)-mediated nick end labeling assay (TUNEL). In conclusion, the authors have shown that switching off HER-2 may disturb the sensitive balance between cell proliferation and cell death, leading to apoptosis and tumor remission. Tumor remission was

dependent on the volume of the tumors before down-regulation of HER-2/neu.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:202649 HCAPLUS
DOCUMENT NUMBER: 138:238205
TITLE: Preparation of fused indoles as anticancer drugs.
INVENTOR(S): Weinberger, Heinz; Beckers, Thomas; Schmidt, Mathias; **Baasner, Silke**; Nickel, Bernd
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020731	A1	20030313	WO 2002-EP9539	20020827
W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RO, RU, SG, SI, SK, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
DE 10143079	A1	20030515	DE 2001-10143079	20010903
CA 2458399	AA	20030313	CA 2002-2458399	20020827
EP 1423393	A1	20040602	EP 2002-767436	20020827
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012300	A	20041013	BR 2002-12300	20020827
CN 1551885	A	20041201	CN 2002-817263	20020827
NZ 531642	A	20050128	NZ 2002-531642	20020827
JP 2005508898	T2	20050407	JP 2003-525001	20020827
US 2004039197	A1	20040226	US 2002-233135	20020830
ZA 2004001290	A	20040323	ZA 2004-1290	20040218
NO 2004000831	A	20040413	NO 2004-831	20040225
PRIORITY APPLN. INFO.:			DE 2001-10143079 A	20010903
			US 2001-317102P P	20010904
			WO 2002-EP9539 W	20020827

OTHER SOURCE(S): MARPAT 138:238205
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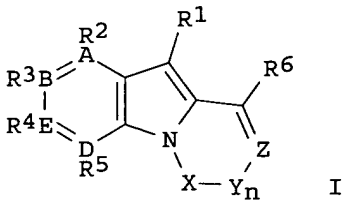

I

AB Title compds. [I; R1 = H, (substituted) aryl, heteroaryl, cycloalkyl, alkyl; A, B, D, E = C, N; R2-R5 = electron pair, H, halo, cyano, NO2, OH, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylcarbonyloxy, alkylsulfonyl, CO2H, amino, etc.; R6, R7, R8 = (substituted) aryl, heteroaryl, cycloalkyl, alkyl; X = CO, SO, SO2; Y = O, NR7; n = 0, 1; Z = CR8], were

prepared Thus, reaction of (5-methoxy-1H-indol-2-yl) Ph methanone oxime (preparation given) with carbonyldiimidazole in refluxing THF gave 5-methoxy-3-phenyl-1,2,5-oxadiazino[4,5-a]indol-6-one. This at 3.16 μg/mL showed 90.7% antiproliferative activity against HeLa/KB in an XTT cytotoxicity test.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:80889 HCAPLUS
DOCUMENT NUMBER: 136:272658
TITLE: Bis(1H-2-indolyl)methanones as a Novel Class of Inhibitors of the Platelet-Derived Growth Factor Receptor Kinase
AUTHOR(S): Mahboobi, Siavosh; Teller, Steffen; Pongratz, Herwig; Hufsky, Harald; Sellmer, Andreas; Botzki, Alexander; Uecker, Andrea; Beckers, Thomas; **Baasner, Silke**; Schaechtele, Christoph; Ueberall, Florian; Kassack, Matthias U.; Dove, Stefan; Boehmer, Frank-D.
CORPORATE SOURCE: Faculty of Chemistry and Pharmacy, Institute of Pharmacy, University of Regensburg, Regensburg, D-93040, Germany
SOURCE: Journal of Medicinal Chemistry (2002), 45(5), 1002-1018
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:272658

AB The novel lead bis(1H-2-indolyl)methanone inhibits autophosphorylation of platelet-derived growth factor (PDGF) receptor tyrosine kinase in intact cells. Various substituents in the 5- or 6-position of one indole ring increase or preserve potency, whereas most modifications of the ring structures and of the methanone group as well as substitution at both indoles result in weak or no activity. An ATP binding site model, derived by homol. from the FGFR-1 tyrosine kinase crystal structure suggesting hydrogen bonds of one indole NH and the methanone oxygen with the backbone carbonyl and amide, resp., of Cys684, explains why only one indole moiety is open for substitution and locates groups in the 5- or 6-position outside the pocket. Some of the most active derivs., inhibit both isoforms of the PDGF receptor kinase in intact cells, with IC50 of 0.1-0.3 μM, and purified PDGFβ-receptor in vitro, with IC50 of 0.09, 0.1, or 0.02 μM, resp. PDGF-stimulated DNA synthesis is inhibited by these derivs. with IC50 values of 1-3 μM. Kinetic anal. of one compound showed an ATP-competitive mode of inhibition. The compds. are inactive or weakly active toward a number of other tyrosine kinases, including the FGF receptor 1, EGF receptor, and c-Src kinase, as well as toward serine-threonine kinases, including different PKC isoforms and GRK2, and appear therefore selective for PDGF receptor inhibition.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:836852 HCAPLUS
DOCUMENT NUMBER: 136:112229
TITLE: Synthetic 2-Aroylindole Derivatives as a New Class of Potent Tubulin-Inhibitory, Antimitotic Agents
AUTHOR(S): Mahboobi, Siavosh; Pongratz, Herwig; Hufsky, Harald; Hockemeyer, Joerg; Frieser, Markus; Lyssenko, Alexei; Paper, Dietrich H.; Buergermeister, Jutta; Boehmer,

Frank-D.; Fiebig, Heinz-Herbert; Burger, Angelika M.; **Baasner, Silke**; Beckers, Thomas
CORPORATE SOURCE: Faculty of Chemistry and Pharmacy Institute of Pharmacy, University of Regensburg, Regensburg, D-93040, Germany
SOURCE: Journal of Medicinal Chemistry (2001), 44(26), 4535-4553
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:112229

AB A new class of simple synthetic antimitotic compds. based on 2-aroylindoles was discovered. (5-Methoxy-1H-2-indolyl)-phenylmethanone (I) as well as analogous 3-fluorophenyl- and 3-methoxyphenyl derivs. displayed high cytotoxicity of IC50 = 20 to 75 nM against the human HeLa/KB cervical, SK-OV-3 ovarian, and U373 astrocytoma carcinoma cell lines. The inhibition of proliferation correlated with the arrest in the G2/M phase of the cell cycle. In in vitro assays with tubulin isolated from bovine brain, in general antiproliferative activity correlated with inhibition of tubulin polymerization Thus, the antimitotic activity of 2-aroylindoles is explained by interference with the mitotic spindle apparatus and destabilization of microtubules. In contrast to colchicine, vincristine, nocodazole, or taxol, I did not significantly affect the GTPase activity of β-tubulin. Interestingly, selected compds. inhibited angiogenesis in the chorioallantoic membrane (CAM) assay. In xenograft expts., I was highly active after oral administration at 200 mg/kg against the human amelanocytic melanoma MEXF 989 in athymic nude mice. We conclude, that 2-aroylindoles constitute an interesting new class of antitubulin agents with the potential to be clin. developed for cancer treatment.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:816437 HCAPLUS
DOCUMENT NUMBER: 135:352771
TITLE: (Hetero)indole derivatives, their preparation, pharmaceutical compositions, and their use as antitumor agents
INVENTOR(S): Beckers, Thomas; **Baasner, Silke**; Klenner, Thomas; Mahboobi, Siavosh; Pongratz, Herwig; Frieser, Markus; Hufsky, Harald; Hockemeyer, Jorg; Fiebig, Heinz-Herbert; Burger, Angelika; Bohmer, Frank-D.
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082909	A2	20011108	WO 2001-EP4783	20010427
WO 2001082909	A3	20020314		

W: AT, AU, BG, BR, BY, CA, CH, CN, CO, CZ, DE, DK, DZ, EE, ES, FI, GB, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LU, LV, MK, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, TR, UA, US, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

DE 10020852	A1	20011031	DE 2000-10020852		20000428
DE 10102629	A1	20020725	DE 2001-10102629		20010120
CA 2407677	AA	20021028	CA 2001-2407677		20010427
EP 1276720	A2	20030122	EP 2001-947247		20010427

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR

BR 2001010414	A	20030211	BR 2001-10414		20010427
JP 2004501092	T2	20040115	JP 2001-579784		20010427
EE 200200607	A	20040415	EE 2002-607		20010427
NO 2002005150	A	20021216	NO 2002-5150		20021025
BG 107309	A	20030930	BG 2002-107309		20021125
PRIORITY APPLN. INFO.:			DE 2000-10020852	A	20000428
			DE 2001-10102629	A	20010120
			WO 2001-EP4783	W	20010427

OTHER SOURCE(S): CASREACT 135:352771; MARPAT 135:352771

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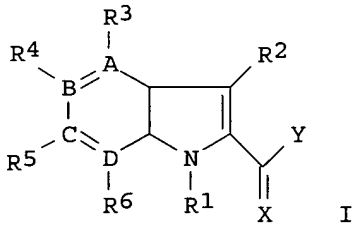

I

AB The invention discloses indole and heteroindole derivs. I [R1 = H, C1-6 alkyl, C1-6 alkylcarbonyl, etc.; R2 = H, halo, cyano, etc.; R3-R6 = H, halo, nitro, etc.; A-D = C, N; Y = (un)substituted C6-14 aryl, etc.; X = O, S, NH, CHOH], and tautomers, stereoisomers, mixts. and salts thereof, as well as the production thereof and the use thereof for the treatment of tumors.

L31 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:795073 HCAPLUS
DOCUMENT NUMBER: 135:331343
TITLE: Preparation of 1H-indol-2-yl aryl ketones and related compounds as antitumor agents
INVENTOR(S): Beckers, Thomas; **Baasner, Silke**; Klenner, Thomas; Mahboobi, Siavosh; Pongratz, Herwig; Frieser, Markus; Hufsky, Harald; Hockemeyer, Joerg; Fiebig, Heinz-Herbert; Burger, Angelika; Boehmer, Frank-D.
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: Ger. Offen., 34 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10020852	A1	20011031	DE 2000-10020852	20000428
WO 2001082909	A2	20011108	WO 2001-EP4783	20010427
WO 2001082909	A3	20020314		

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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

US 2002091124	A1	20020711	US 2001-843139		20010427
CA 2407677	AA	20021028	CA 2001-2407677		20010427
EP 1276720	A2	20030122	EP 2001-947247		20010427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, TR					
BR 2001010414	A	20030211	BR 2001-10414		20010427
JP 2004501092	T2	20040115	JP 2001-579784		20010427
EE 200200607	A	20040415	EE 2002-607		20010427
US 2003158216	A1	20030821	US 2002-279123		20021024
NO 2002005150	A	20021216	NO 2002-5150		20021025
ZA 2002009137	A	20040618	ZA 2002-9137		20021111
BG 107309	A	20030930	BG 2002-107309		20021125
PRIORITY APPLN. INFO.:			DE 2000-10020852	A	20000428
			DE 2001-10102629	A	20010120
			US 2001-843139	B1	20010427
			WO 2001-EP4783	W	20010427

OTHER SOURCE(S): MARPAT 135:331343
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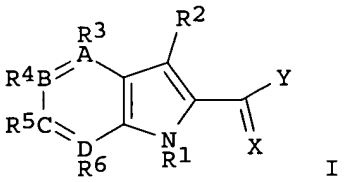
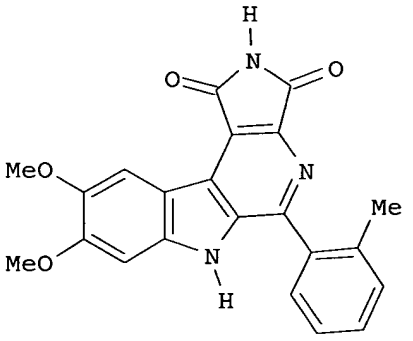


I

AB Use of title compds. [I; R1 = H, alkylcarbonyl, alkylaminoalkyl, dialkylaminoalkyl, (hetero)cyclyl; R2 = H, halo, cyano, NO2, (substituted) alkyl, alkoxy, etc.; A-D = N, (substituted) C; R3-R6 = free electron pair if A-D = N, or H, halo, cyano, NO2, alkyl, etc. if A-D = C; Y = (substituted) aryl; X = O, S, NH, (H,OH)], for preparation of drugs for treatment of tumor illness in mammals is claimed. Thus, 5-methoxy-1H-indol-2-yl Ph ketone (general preparation given) showed antitumor activity with IC50 = 96.5 nM in rat glioma cell lines C6.

L31 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:398021 HCAPLUS
DOCUMENT NUMBER: 133:164199
TITLE: Pyrrolo[3,4-c]-β-carboline-diones as a novel class of inhibitors of the platelet-derived growth factor receptor kinase
AUTHOR(S): Teller, Steffen; Eluwa, Stella; Koller, Markus; Uecker, Andrea; Beckers, Thomas; **Baasner, Silke**; Bohmer, Frank-D.; Mahboobi, Siavosh
CORPORATE SOURCE: Research Unit Molecular Cell Biology, Medical Faculty, Friedrich Schiller University, Jena, D-07747, Germany
SOURCE: European Journal of Medicinal Chemistry (2000), 35(4), 413-427
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Members of the structurally diverse family of β-carbolines have previously been shown to exhibit a wide range of biol. activities. A novel synthetic strategy for generation of β-carbolines was developed, allowing imido-β-carbolines to be created in three steps from known compds. The compds. were screened for inhibition of platelet-derived growth factor (PDGF)-stimulated tyrosine phosphorylation in Swiss 3T3 fibroblasts. A number of the newly synthesized β-carbolines with moderate to potent inhibitory activity were revealed. β-Carboline I was found to be the most active derivative inhibiting purified PDGF receptor kinase and PDGF-receptor autophosphorylation in intact cells with IC50 values of 0.4 and 2.6 μM, resp. I also inhibited PDGF-stimulated DNA synthesis in Swiss 3T3 fibroblasts with an IC50 of 3.2 μM. The compound had no effect on Src or epidermal growth factor (EGF) receptor kinase activity and a six-seven-fold higher IC50 for inhibition of basic fibroblast growth factor (bFGF)-stimulated tyrosine phosphorylation or Kit/stem cell factor (SCF) receptor autophosphorylation, indicating a reasonable extent of kinase specificity. Thus, β-carbolines present a new lead of tyrosine kinase inhibitors with the capacity to selectively interfere with PDGF receptor signal transduction and PDGF-dependent cell growth.
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:242550 HCAPLUS
DOCUMENT NUMBER: 133:236049
TITLE: A refined model for monitoring orthotropic tumor growth in nude mice
AUTHOR(S): Klenner, T.; Beckers, T.; Westhof, A.; **Baasner, S.**; Hilgard, P.
CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, Germany
SOURCE: Contributions to Oncology (1999), 54(Relevance of Tumor Models for Anticancer Drug Development), 101-108
CODEN: COONEV; ISSN: 0250-3220
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Athymic nude mice are commonly used in cancer research as hosts for xenografts of human tumors or oncogene-transformed recombinant cell lines. Tumorigenesis induced by the receptor tyrosine kinase HER2 was studied in vivo using the tTA/tetO7 system to allow conditional HER2 overexpression in NIH 3T3 fibroblasts. The tetoff system allows for a differential control of gene expression which is switched off by increasing concns. of tetracyclines. Because the expression of HER2 is related to the marker gene human secreted placental-type alkaline phosphatase (SEAP), tumor cell growth can be monitored in vitro and in vivo by simply measuring SEAP in culture supernatants or animal serum. Thus, a target-specific xenograft model was developed. However, it might be possible to use SEAP in other cell lines. Hence, the surgical methods were combined with the mol. biol. methods. SEAP was employed as a reporter gene for transfection of human tumor cell lines to develop a more sensitive, reliable and generally applicable method for monitoring tumor growth in nude mice independent of the location of the tumor.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:351174 HCAPLUS
DOCUMENT NUMBER: 126:312250
TITLE: Tumor cell lines using the human placenta-specific alkaline phosphatase gene as a reporter in the screening of antitumor-compositions
INVENTOR(S): Beckers, Thomas; Klenner, Thomas; **Baasner, Silke**
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany; Zentaris GmbH; Asta Medica Oncology GmbH & Co.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 773293	A2	19970514	EP 1996-117448	19961030
EP 773293	A3	19981230		
EP 773293	B1	20031203		
R: CH, DE, FR, GB, LI				
DE 19542051	A1	19970515	DE 1995-19542051	19951110
DE 19542051	C2	20000323		
US 5837462	A	19981117	US 1996-746383	19961108
JP 09131184	A2	19970520	JP 1996-312624	19961111

PRIORITY APPLN. INFO.: DE 1995-19542051 A 19951110

AB Tumor cell lines carrying an expression cassette for the secreted human placental alkaline phosphatase (SEAP) are described for use in the screening of compds. for their effectiveness as antitumor compds. These cells can be used for implantation into a test animal or in culture. Serum levels of the enzyme are proportional to the number of cells in the animal and can be used to measure rates of tumor growth before the tumor forms a palpable mass. Dicistronic expression constructs are used. The constructs use a constitutive or inducible promoter to drive expression of a gene that can induce tumorigenic growth of cells, e.g. erb2/HER2, an IRES, and the gene for SEAP with the two genes in any oder. The development of an in vivo system using the c-erbB2 gene in a dicistronic construct with the SEAP gene is described. A constitutive expression cassette using the SV40 immediate-early promoter and an inducible cassette using a

tetracycline-responsive operator are described.

L31 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:612409 HCAPLUS
DOCUMENT NUMBER: 125:272260
TITLE: Reversible tumorigenesis in mice by conditional expression of the HER2/c-erbB2 receptor tyrosine kinase
AUTHOR(S): **Baasner, Silke**; von Melchner, Harald; Klenner, Thomas; Hilgard, Peter; Beckers, Thomas
CORPORATE SOURCE: Department of Cancer Research, ASTA Medica AG, Frankfurt/Main, 60314, Germany
SOURCE: Oncogene (1996), 13(5), 901-911
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present study we describe the reversible transformation of NIH3T3 fibroblasts by overexpression of the HER2/c-erbB2 receptor tyrosine kinase. Cell lines expressing HER2 under control of a tetracycline-responsive promotor were isolated. Induction of HER2 expression resulted in cellular transformation in vitro as depicted by growth in soft agar and focus formation in tissue culture. Subsequent treatment of these cells with the effector anhydrotetracylin switched-off HER2 expression and induced morphol. and functional changes characteristic for non-transformed cells. S.c. transplantation of cells in nude mice resulted in the formation of solid tumors. Interestingly tumor formation was completely suppressed by treatment of the animals with anhydrotetracyline. Our findings indicate that overexpression of HER2 induces the transformed phenotype of NIH3T3 cells and is required for tumor formation and progression in nude mice. By linking the expression of the marker gene secreted placental alkaline phosphatase to the expression of HER2, a sensitive monitoring of tumor development in nude mice was feasible.

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L40           76 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L38 AND (?TUMOR? OR ?CANCER?
                OR ?NEOPLAS? OR ?PROLIFER? OR ?CHEMOPREV?)
L41           69 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L35 OR L39 OR L40) NOT (L20
                OR L23 OR L25 OR L31)


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L41  ANSWER 1 OF 69  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2005:581409  HCAPLUS
TITLE:                    Polysomy 8 defines a clinico-cytogenetic entity
                          representing a subset of myeloid hematologic
                          malignancies associated with a poor prognosis:
                          report on a cohort of 12 patients and review of 105
                          published cases
AUTHOR(S):                Beyer, Valerie; Muehlematter, Dominique; Parlier,
                          Valerie; Cabrol, Christine; Bougeon-Mamin, Sandrine;
                          Solenthaler, Max; Tobler, Andreas; Pugin, Paul;
                          Gregor, Michael; Hitz, Felicitas; Hess, Urs; Chapuis,
                          Bernard; Laurencet, France; Schanz, Urs; Schmidt,
                          Pierre-Michel; van Melle, Guy; Jotterand, Martine
CORPORATE SOURCE:         Unite de cytogenetique du cancer, Service de genetique
                          medicale, Centre Hospitalier Universitaire Vaudois
                          (CHUV), Lausanne, CH-1011, Switz.
SOURCE:                   Cancer Genetics and Cytogenetics (2005), 160(2),
                          97-119
                          CODEN: CGCYDF; ISSN: 0165-4608
PUBLISHER:                Elsevier Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Tetrasomy, pentasomy, and hexasomy 8 (polysomy 8) are relatively rare
     compared to trisomy 8.  Here we report on a series of 12 patients with
     acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), or
     myeloproliferative disorder (MPD) associated with polysomy 8 as
     detected by conventional cytogenetics and fluorescence in situ
     hybridization (FISH).  In an attempt to better characterize the clin. and
     hematol. profile of this cytogenetic entity, our data were combined with
     those of 105 published patients.  Tetrasomy 8 was the most common
     presentation of polysomy 8.  In 60.7% of patients, polysomy 8 occurred as
     part of complex changes (16.2% with 11q23 rearrangements).  No cryptic MLL
     rearrangements were found in cases in which polysomy 8 was the only
     karyotypic change.  Our study demonstrates the existence of a polysomy 8
     syndrome, which represents a subtype of AML, MDS, and MPD characterized by
     a high incidence of secondary diseases, myelomonocytic or monocytic
     involvement in AML and poor overall survival (6 mo).  Age significantly
     reduced median survival, but associated cytogenetic abnormalities did not
     modify it.  Cytogenetic results further demonstrate an in vitro
     preferential growth of the cells with a high level of aneuploidy
     suggesting a selective advantage for polysomy 8 cells.
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L41 ANSWER 2 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:412974 HCAPLUS
DOCUMENT NUMBER: 143:73163
TITLE: Alcohol intake modulates the genetic association between HDL cholesterol and the PPARγ2 Pro12Ala polymorphism
AUTHOR(S): Brand-Herrmann, Stefan-Martin; Kuznetsova, Tatiana; Wiechert, Andreas; Stolarz, Katarzyna; Tikhonoff, Valerie; **Schmidt-Petersen, Klaus**; Telgmann, Ralph; Casiglia, Edoardo; Wang, Ji-Guang; Thijs, Lutgarde; Staessen, Jan A.; Brand, Eva
CORPORATE SOURCE: The European Project on Genes in Hypertension Investigators, Leibniz Institute for Arteriosclerosis Research, University of Muenster, Muenster, Germany
SOURCE: Journal of Lipid Research (2005), 46(5), 913-919
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: American Society for Biochemistry and Molecular Biology, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The peroxisome **proliferator**-activated receptor γ (PPARγ) Pro12Ala polymorphism affects plasma lipids, but to what extent alc. intake interferes with this association remains unknown. The authors randomly recruited 251 nuclear families (433 parents and 493 offspring) in the framework of the European Project on Genes in Hypertension study and genotyped 926 participants in whom all serum lipid variables and information on alc. consumption were available for PPARγ2 Pro12Ala. Genotype-phenotype relations were assessed using generalized estimating equations (GEE) and a quant. transmission disequil. test (QTDT). The Ala 12 allele was more frequent in Novosibirsk (0.17) than in Cracow (0.12) and Mirano (0.11). Using GEE or QTDT, Italian offspring carrying the Ala 12 allele had higher serum HDL cholesterol than noncarriers. HDL cholesterol levels were on average 0.086 mM higher in drinkers than in nondrinkers. Compared with Pro 12 homozygotes, Ala 12 allele carriers consuming alc. had higher serum total and HDL cholesterol, with the opposite trend occurring in nondrinkers. This genotype-alc. interaction was independent of the type of alc. beverage and more pronounced in moderate than in heavy drinkers. The authors conclude that alc. intake modulates the relation between the PPARγ2 Pro12Ala and HDL cholesterol level and that, therefore, the Pro12Ala polymorphism, pending confirmation of the authors' findings, might affect cardiovascular prognosis.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 3 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:120730 HCAPLUS
DOCUMENT NUMBER: 140:157434
TITLE: Use of alkyl phosphocholines in combination with **antitumor** medicaments for the treatment of **benign** and **malignant tumors**
INVENTOR(S): Engel, Jurgen; **Gunther, Eckhard**; Sindermann, Herbert
PATENT ASSIGNEE(S): Zentaris GmbH, Germany
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004012744	A1	20040212	WO 2003-EP8346		20030729
W: AU, BR, BY, CA, CN, CO, GE, HR, ID, IL, IN, IS, JP, KR, KZ, LT, LV, MK, MX, NO, NZ, PH, PL, RU, SG, UA, UZ, YU, ZA					
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR					
CA 2493023	AA	20040212	CA 2003-2493023		20030729
BR 2003013048	A	20050614	BR 2003-13048		20030729
EP 1545553	A1	20050629	EP 2003-766336		20030729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
US 2004097470	A1	20040520	US 2003-632187		20030730
CA 2436332	AA	20050131	CA 2003-2436332		20030731
PRIORITY APPLN. INFO.:			US 2002-399615P	P	20020730
			WO 2003-EP8346	W	20030729

OTHER SOURCE(S): MARPAT 140:157434

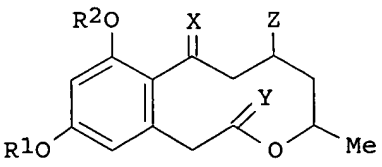
AB The invention discloses the use of alkyl phosphocholines in combination with **antitumor** medicaments for treating **benign** and **malignant tumor** diseases in humans and mammals. The alkyl phosphocholines can be used in combination with one or a combination of several approved cytostatics. Compds. of the invention include e.g. perifosine.

L41 ANSWER 4 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:912847 HCAPLUS
DOCUMENT NUMBER: 139:395749
TITLE: Isolation and synthesis of decalactones from Penicillium species and methods for making pharmaceuticals there from
INVENTOR(S): Bringmann, Gerhard; Proksch, Peter; Edrada, Ru Angelie; Heubes, Markus; **Gunther, Eckhard**
PATENT ASSIGNEE(S): Biotecmarin GmbH, Germany
SOURCE: U.S. Pat. Appl. Publ., 8 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003216354	A1	20031120	US 2002-143596	20020509
US 6872747	B2	20050329		
PRIORITY APPLN. INFO.:			US 2002-143596	20020509

OTHER SOURCE(S): CASREACT 139:395749; MARPAT 139:395749
GI



I

AB A novel class of decalactones I [R1 = H, (un)branched C1-6-alkyl or C1-6-alkyl mono- or multisubstituted by C6-14-aryl, (un)branched carboxy(C1-18-alkyl), (un)branched (C1-6-alkoxy)carbonyl, (un)branched (C1-12-alkyl)carbonyl, C2-6-alkenyl, C2-6-alkynyl, (un)branched cyano(C1-18-alkyl), OCH2Ph, (9-fluorenylmethoxy)carbonyl (Fmoc), CPh3, 2-(4-pyridyl)ethoxycarbonyl (Pyoc), SiPh2Me (DPMS); R2 = R1; X = O, S, NOH, NOR4; Y = O, S; Z = H, OR3 ; R3 = R1; R4 = (un)branched C1-6-alkyl or C1-6-alkyl mono- or multisubstituted by C6-14-aryl, (un)branched carboxy(C1-18-alkyl), (un)branched (C1-6-alkoxy)carbonyl, (un)branched (C1-12-alkyl)carbonyl], and their enantiomers [R, S] or stereoisomers [(R,R), (R,S), (S,S)] or mixts. thereof, and a method for their isolation is disclosed. Thus, xestodecalactone A [(+)-I; R1 = R2 = H, X = Y = O, Z = H] was isolated from fungus of Penicillium sp. found on freshly collected samples of marine sponge Xestospongia exigua. A method for the synthesis of the decalactones I and the use of the decalactones in pharmaceutical compns. is also described. Thus, (±)-I [R1 = R2 = H, X = Y = O, Z = H] was prepared from 3,5-(HO)2C6H3CH2CO2Me and MeC(:O)(CH2)3CO2H via coupling of 3,5-(PhCH2O)2C6H3CH2CO2H with MeC(OH)(CH2)3CO2Me and intramol. acylation of 3,5-(PhCH2O)2C6H3CH2CO2CHM3(CH2)3CO2H, followed by hydrogenolytic debenzylation. The **antitumor** activity of I (0.003 - 3.16 μg) was determined (no data).

L41 ANSWER 5 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:473458 HCAPLUS
DOCUMENT NUMBER: 139:179863
TITLE: Novel Benzylidene-9(10H)-anthracenones as Highly Active Antimicrotubule Agents. Synthesis, **Antiproliferative** Activity, and Inhibition of Tubulin Polymerization
AUTHOR(S): Prinz, Helge; Ishii, Yukihito; Hirano, Takeo; Stoiber, Thomas; Gomez, Juan A. Camacho; **Schmidt, Peter** ; Duessmann, Heiko; Burger, Angelika M.; Prehn, Jochen H. M.; Guenther, Eckhard G.; Unger, Eberhard; Umezawa, Kazuo
CORPORATE SOURCE: Institute of Pharmaceutical and Medicinal Chemistry, Westphalian Wilhelms-University, Muenster, D-48149, Germany
SOURCE: Journal of Medicinal Chemistry (2003), 46(15), 3382-3394
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:179863
AB A novel series of 10-benzylidene-9(10H)-anthracenones and 10-(phenylmethyl)-9(10H)-anthracenones were synthesized and evaluated for **antiproliferative** activity in an assay based on K562 leukemia cells. The 3-hydroxy-4-methoxybenzylidene analog (I) was found to be the most active compound (IC50 K562: 20 nM). Structure-activity relationships are also considered. The highly active compound I and the 2,4-dimethoxy-3-hydroxybenzylidene analog (II) were tested against five **tumor** cell lines using the XTT assay, including multidrug resistant phenotypes. Induction of cell death in a variety of **tumor** cell lines was determined in a monolayer assay using propidium iodide. Noteworthy, all compds. within the series induced elongations in K562 cells similar to vinblastine-treated cells. The effect of the lead compound I on K562 cell growth was associated with cell cycle arrest in G2/M.

Concns. for 50% KB/HeLa cells arrested in G2/M after treatment with I and II were determined and found to be in the range of 0.2 μM. Addnl., the dose dependent caspase-3-like protease activity was monitored in K562 cells and MCF-7/Casp-3 cells treated with I, indicating induction of apoptosis. Western blotting anal. demonstrated that I caused a shift in tubulin concentration from the polymerized state found in the cell pellet to the unpolymd. state found in the cell supernatant. Seven compds. strongly inhibited tubulin polymerization with activities higher or comparable to those of the reference compds. such as colchicine, podophyllotoxin, and nocodazole. In general, the **antiproliferative** activity correlated with inhibition of tubulin polymerization The most active compds. strongly displaced [3H]colchicine from its binding site in the tubulin, yielding IC50 values 3- to 4-fold lower than that of colchicine. The novel benzylidene-9(10H)-anthracenones described in the present study constitute an interesting group of highly active and easily accessible antimitotic agents that inhibit tubulin polymerization

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 6 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:414842 HCAPLUS
DOCUMENT NUMBER: 139:226932
TITLE: Evariquinone, isoemericellin, and stromemycin from a sponge derived strain of the fungus Emericella variecolor
AUTHOR(S): Bringmann, Gerhard; Lang, Gerhard; Steffens, Stefan; **Gunther, Eckhard**; Schaumann, Karsten
CORPORATE SOURCE: Institut fuer Organische Chemie der Universitaet, Wuerzburg, D-97074, Germany
SOURCE: Phytochemistry (Elsevier) (2003), 63(4), 437-443
CODEN: PYTCAS; ISSN: 0031-9422
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB From a strain of the fungus Emericella variecolor derived from the marine sponge Haliclona valliculata, two new natural products, evariquinone and isoemericellin, were isolated after HPLC-UV, -MS, and -NMR studies of the extract and their structures were elucidated by mass spectrometry and NMR expts. Evariquinone showed **antiproliferative** activity towards KB and NCI-H460 cells at a concentration of 3.16 μg/mL. Furthermore, the fungus was found to produce the known metabolites stromemycin, shamixanthone, and 7-hydroxyemodin. Chemical degradation, NMR decoupling expts., and spin-system simulation provided evidence for the double bonds in stromemycin to be all E-configured. ROESY expts. established the monosaccharide moiety to be glucose.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 7 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:355269 HCAPLUS
DOCUMENT NUMBER: 138:400363
TITLE: A new murine model of islet xenograft rejection: Graft destruction is dependent on a major histocompatibility-specific interaction between T-cells and macrophages
AUTHOR(S): **Schmidt, Peter**; Krook, Henrik; Maeda, Akira;

Korsgren, Olle; Benda, Birgitta
CORPORATE SOURCE: Division of Clinical Immunology, Uppsala University, Uppsala, SE-75185, Swed.
SOURCE: Diabetes (2003), 52(5), 1111-1118
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new murine model of porcine islet-like cell cluster (ICC) xenograft rejection, avoiding interference of unspecific inflammation, was introduced and used to investigate rejection mechanisms. Athymic (nu/nu) mice were transplanted with syngeneic, allogeneic, or xenogeneic islets under the kidney capsule. After the original transplantation, immune cells in porcine ICC xenografts undergoing rejection in native immunocompetent mice were transferred to the peritoneal cavity of the athymic mice. At defined time points after transfer, the primary grafts were evaluated by immunohistochem. and real-time quant. RT-PCR to estimate cytokine and chemokine mRNA expression. Transfer of immunocompetent cells enabled athymic (nu/nu) mice to reject a previously tolerated ICC xenograft only when donor and recipient were matched for major histocompatibility complex (MHC). In contrast, allogeneic and syngeneic islets were not rejected. The ICC xenograft rejection was mediated by transferred T-cells. The main effector cells, macrophages, were shown to be part of a specific immune response. By day 4 after transplantation, there was an upregulation of both Th1- and Th2-associated cytokine transcripts. The transferred T-cells were xenospecific and required MHC compatibility to induce rejection. Interaction between the TCR of transferred T-cells and MHC on host endothelial cells and/or macrophages seems necessary for inducing ICC xenograft rejection.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 8 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:10813 HCAPLUS
DOCUMENT NUMBER: 139:2695
TITLE: Real-time determination of telomerase activity in cell extracts using an optical biosensor
AUTHOR(S): **Schmidt, Peter M.**; Matthes, Eckart; Scheller, Frieder W.; Bienert, Michael; Lehmann, Christine; Ehrlich, Angelika; Bier, Frank F.
CORPORATE SOURCE: Fraunhofer-Institut fur Biomedizinische Technik, Abt. Molekulare Bioanalytik und Bioelektronik, Potsdam-Rehbrucke, D-14558, Germany
SOURCE: Biological Chemistry (2002), 383(10), 1659-1666
CODEN: BICHF3; ISSN: 1431-6730
PUBLISHER: Walter de Gruyter GmbH & Co. KG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A biosensoric approach has been developed to determine the activity of telomerase in **tumor** cell lysates. An optical sensor, the grating coupler, was used to monitor the association and dissociation of unlabeled compds. on the sensor surface in real time, by virtue of an evanescent field. An oligonucleotide was immobilized on the surface of the optical biosensor and linked with two other oligonucleotides by complementary sequences in an overlapping manner. The 3'-end of the last one carried the sequence of the telomeric substrate (TS) primer used for elongation by telomerase in the telomeric repeat amplification protocol (TRAP) assay. This primer sequence was phosphorothioate (PS)-modified, which is known to strongly increase the affinity to the primer binding site of telomerase

protein and consequently the velocity of the telomerase reaction. We show that the PS primer binds to the modified biosensor and is elongated effectively by the telomerase from HL-60 cell lysates. A synthesis rate of 1 nucleotide/min was determined The inhibitory effect of peptide nucleic acid (PNA) was shown by using immobilized TS. The velocity of the telomerase reaction was slowed down and the signal intensity was below the signal-to-noise ratio. Most nucleic acid detection systems use amplification steps such as polymerase chain reaction (PCR) to increase the amount of the probe. Since telomerase is a polymerase itself amplification of DNA by PCR is not required. Furthermore, no purification steps were required since all measurements were performed with crude cell extract

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 9 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:801364 HCAPLUS
DOCUMENT NUMBER: 138:35083
TITLE: Detection of activity of telomerase in **tumor** cells using fiber optical biosensors
AUTHOR(S): **Schmidt, Peter M.**; Lehmann, Christine; Matthes, Eckart; Bier, Frank F.
CORPORATE SOURCE: Abt. Molekulare Bioanalytik und Bioelektronik, Fraunhofer-Institut fur Biomedizinische Technik, Potsdam-Rehbrucke, 14558, Germany
SOURCE: Biosensors & Bioelectronics (2002), 17(11-12), 1081-1087
CODEN: BBIOE4; ISSN: 0956-5663
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human telomerase plays an important role in the **cancerogenesis** as it is up-regulated in 80-90% of **malignant tumors.** Thus, it is considered as a potential **cancer** marker and relevant target in oncol. Its task is the extension of guanine-rich strands of the telomere using an intrinsic RNA as the template. In this paper we developed a new biosensor assay based on total internal reflection fluorescence measuring the activity of the telomerase on sensor surface. Two alternatives to determine the telomeric activity are demonstrated without the use of amplifying steps as e.g. PCR. The enzymic inclusion of FITC-labeled dUTPs should reveal the synthesis process in real-time indicating the elongation of a phosphothioate telomeric substrate (PS/TS)-modified primer. Addnl. the elongated strand was detected by hybridization with a FITC-labeled complementary linear DNA probe. As the telomeric guanine-rich single-stranded DNA adopts intramol. quadruplex structures, it was necessary for the hybridization to linearize the telomeric DNA by increasing the reaction temperature to 48 °C. The comparison of the telomerase activity using labeled and unlabeled nucleotides indicated the inhibition effect of the FITC-labeled nucleotides slowing down the synthesis rate of the enzyme. It is shown with the modified biosensor that the PS/TS primer binds the telomerase from the HL-60 cell lysates, effectively elongating the immobilized primer. Furthermore no more purification steps were required as all measurements were performed with crude cell extract
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 10 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:43292 HCAPLUS
DOCUMENT NUMBER: 136:230318

TITLE: Tenascin-C aptamers are generated using **tumor** cells and purified protein
AUTHOR(S): Hicke, Brian J.; Marion, Chris; Chang, Ying-Fon; Gould, Ty; Lynott, Cynthia K.; Parma, David; **Schmidt, Paul G.**; Warren, Steve
CORPORATE SOURCE: SomaLogic, Boulder, CO, 80301, USA
SOURCE: Journal of Biological Chemistry (2001), 276(52), 48644-48654
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Tenascin-C (TN-C) is an extracellular matrix protein that is overexpressed during tissue remodeling processes, including **tumor** growth. To identify an aptamer for testing as a **tumor**-selective ligand, SELEX (systematic evolution of ligands by exponential enrichment) procedures were performed using both TN-C and TN-C-expressing U251 glioblastoma cells. The different selection techniques yielded TN-C aptamers that are related in sequence. In addition, a crossover procedure that switched from **tumor** cell to purified protein selections was effective in isolating two high-affinity TN-C aptamers. When targeting **tumor** cells in vitro, the observed propensity of naive oligonucleotide pools to evolve TN-C aptamers may be due to the abundance of this protein. In vivo, TN-C abundance may also be well suited for aptamer accumulation in the **tumor** milieu. A size-minimized and nuclease-stabilized aptamer, TTA1, binds to the fibrinogen-like domain of TN-C with an equilibrium dissociation constant (Kd) of 5 x 10-9 M. At 13 kDa, this aptamer is intermediate in size between peptides and single chain antibody fragments, both of which are superior to antibodies for **tumor** targeting because of their smaller size. TTA1 defines a new class of ligands that are intended for targeted delivery of radioisotopes or chemical agents to diseased tissues.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 11 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:27422 HCAPLUS
DOCUMENT NUMBER: 137:104289
TITLE: Detection of **tumor** cells in peritoneal lavages from patients with gastrointestinal **cancer** by multiplex reverse transcriptase PCR
AUTHOR(S): **Schmidt, Petra**; Thiele, Mariana; Rudroff, Claudia; Vaz, Alexandra; Schilli, Margret; Friedrich, Karlheinz; Scheele, Johannes
CORPORATE SOURCE: Department of Surgery, Friedrich-Schiller-University Jena, Jena, D-07740, Germany
SOURCE: Hepato-Gastroenterology (2001), 48(42), 1675-1679
CODEN: HEGAD4; ISSN: 0172-6390
PUBLISHER: H.G.E. Update Medical Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytol. examination of peritoneal lavages is a useful predictor of peritoneal recurrence in gastrointestinal carcinoma patients. Nevertheless, it may be inadequate for those patients with lavages containing only few **cancer** cells. In the present study, sensitive detection of free **cancer** cells could be achieved through amplification of cytokeratin 19, carcinoembryonic antigen, α-fetoprotein mRNAs by means of multiplex reverse transcriptase polymerase chain reaction and

nested polymerase chain reaction. The multiplex reverse transcriptase polymerase chain reaction assay was used to examine lavage samples from 64 patients with various gastrointestinal **malignant** lesions (colorectal n=27; duodenal carcinoma n=1; gastric n=7; pancreatic n=4; hepatocellular carcinoma n=2; gallbladder n=1; cholangiocellular carcinoma n=2 and 20 colorectal liver metastases). Specificity was assessed by examination of 15 donors without **malignancies.** In addition, nested polymerase chain reaction was used to improve the sensitivity of the assay for the detection of α-fetoprotein transcripts. Peritoneal lavages from 12 of 64 gastrointestinal carcinoma patients were pos. for carcinoembryonic antigen mRNA. Carcinoembryonic antigen proved a specific marker, as no false-positives were detected in any patients without gastrointestinal **cancer.** α-Fetoprotein mRNA was detected exclusively in peritoneal lavages from **tumor** patients, i.e., in 16 of 27 colon **cancer** patients, 14 of 20 patients with colorectal liver metastasis, 2 of 7 patients with gastric **cancer** , two patients with hepatocellular carcinoma and 2 of 4 patients with pancreatic **cancer.** Cytokeratin 19 mRNA was not found a useful marker, since control patients without **malignancies** were also pos. Our data suggest that carcinoembryonic antigen- and α-fetoprotein mRNA in peritoneal lavage are potentially useful specific markers for early diagnosis of metastasis of gastrointestinal **cancer.** It has been shown that α-fetoprotein-specific nested reverse transcriptase polymerase chain reaction can detect not only hepatocellular carcinoma cells, but also **malignant** cells from other gastrointestinal carcinomas. In contrast, cytokeratin 19 mRNA lacks specificity for gastrointestinal **cancer.**

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 12 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:598438 HCAPLUS
DOCUMENT NUMBER: 135:134311
TITLE: Screen for risk for gastric adenocarcinoma
INVENTOR(S): Goldenring, James R.; **Schmidt, P. Henry;** Lee, Jeffrey R.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 6 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001014459	A1	20010816	US 1998-164954	19981001
US 6372439	B2	20020416		
US 2002187487	A1	20021212	US 2002-60113	20020129
US 6773890	B2	20040810		

PRIORITY APPLN. INFO.: US 1998-164954 A3 19981001

AB It has been determined that a specific metaplastic lineage that contains immunoreactivity for a trefoil polypeptide, spasmolytic peptide, is associated with and gives rise to the vast majority of human adenocarcinomas. The identification of this Spasmolytic Polypeptide Expressing Metaplasia (SPEM) is a major factor for grading of biopsies of the stomach to assess risk for gastric **cancer.** It also forms the basis of a method for serol. screening for those at risk for gastric **cancer.** In a preferred embodiment, antibodies to spasmolytic peptide (hSP) are used in immunostaining of biopsies of gastric tissue obtained by endoscopy for

grading biopsies. Those patients having these cells, characterized by a morphol. more typical of a type of cell present normally in the intestine and not stomach, Brunner's gland cells, are at risk of developing adenocarcinoma. Since these cells express hSP, antibodies or nucleic acid probes hybridizing to mRNA encoding hSP, can be used for rapid detection of the cells in tissue biopsies. The antibodies can also be used in serol. tests for screening and following patients at risk for gastric **cancer.** In combination with evidence of previous or present invention with H. pylori,the tests are predictive of the likelihood of developing adenocarcinoma.

L41 ANSWER 13 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:398301 HCAPLUS
DOCUMENT NUMBER: 135:111531
TITLE: Morphological organ alterations and infectious diseases in brown trout Salmo trutta and rainbow trout Oncorhynchus mykiss exposed to polluted river water
AUTHOR(S): **Schmidt-Posthaus, Heike**; Bernet, Daniel; Wahli, Thomas; Burkhardt-Holm, Patricia
CORPORATE SOURCE: Centre for Fish and Wildlife Health, Institute of Animal Pathology, University of Bern, Bern, 3012, Switz.
SOURCE: Diseases of Aquatic Organisms (2001), 44(3), 161-170
CODEN: DAOREO; ISSN: 0177-5103
PUBLISHER: Inter-Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Poor water quality is discussed as a major factor causing a decline of brown trout populations in Swiss rivers. We selected a river in the Swiss midlands, where the brown trout population has decreased dramatically during the last 10 yr and where feral fish have shown distinctive pathol. alterations. The objective was to study whether river water may be responsible for impaired fish health leading to an increased mortality in the river. In an active monitoring program, groups of brown and rainbow trout were exposed to polluted river water for 24 mo. Fish held in tap water served as a reference Mortality, macroscopic and histopathol. changes, and infectious agents were studied. Compared with the reference group, high mortality rates and severe pathol. alterations of the inner organs were observed in fish held in river water. Especially gills, liver and kidney of these fish showed significantly higher changes than fish from tap water. These changes were dominated by degenerative and inflammatory reactions. Several infectious agents were diagnosed in fish exposed to river water. The most important findings were furunculosis and **proliferative** kidney disease. Brown trout seemed to be more sensitive than rainbow trout to environmental stress and infectious agents.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 14 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:212427 HCAPLUS
DOCUMENT NUMBER: 135:302574
TITLE: Early detection of increased **tumor** necrosis factor alpha (TNFα) and soluble TNF receptor protein plasma levels after trauma reveals associations with the clinical course
AUTHOR(S): Spielmann, S.; Kerner, T.; Ahlers, O.; Keh, D.; **Gerlach, M.**; Gerlach, H.
CORPORATE SOURCE: Department of Anaesthesiology and Intensive Care Medicine, Charite-Virchow Hospital, Humboldt

University, Berlin, Germany
SOURCE: Acta Anaesthesiologica Scandinavica (2001), 45(3), 364-370
CODEN: AANEAB; ISSN: 0001-5172
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The inflammatory response after trauma includes **tumor** necrosis factor alpha (TNFα) as pro-inflammatory cytokine. Furthermore, both soluble TNF receptor proteins (sTNF-R1 and sTNF-R2) were described to influence the post-traumatic inflammatory response and organ dysfunction. From 47 trauma patients, blood samples were obtained at the scene of accident, at hospital admission, after 4 h, 12 h, and 24 h, and daily until day 6. Plasma levels of TNFα, sTNF-R1 and sTNF-R2 were measured by enzyme immunoassay (EIA) and analyzed comparing clin. parameters such as injury scores (ISS, AIS), development of multiple organ dysfunction syndrome (MODS) and/or systemic inflammatory response syndrome (SIRS), and outcome. Significant changes were observed in a time-dependent manner: TNFα and soluble TNF receptor levels were elevated compared to values of healthy persons. At 4 h after trauma, TNFα and sTNF-R2 showed an increase from initial values, which continued during the entire observation period. Severe trauma led to enhanced sTNF-R1 levels on scene and on hospital admission. Development of SIRS along with elevated sTNFR1 began on scene and was present on admission, with increased sTNF-R2 from day 1 to day 4. MODS (until day 6) was preceded by increased sTNF-R2 levels on admission and up to 4 h after trauma. Outcome was associated neither with TNFα nor with soluble TNF receptor levels. Thus, in trauma patients, early post-traumatic MODS and SIRS coincide with increased levels of TNFα and TNF receptor proteins, revealing different, time-dependent changes. Hence, detection of TNFα and soluble TNF receptor proteins after trauma should pay regard to the time point of sampling.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 15 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:119860 HCAPLUS
DOCUMENT NUMBER: 134:278944
TITLE: Cathepsin L deficiency as molecular defect of furless: **hyperproliferation** of keratinocytes and perturbation of hair follicle cycling
AUTHOR(S): Roth, Wera; Deussing, Jan; Botchkarev, Vladimir A.; Pauly-Evers, Meike; Saftig, Paul; Hafner, Angela; **Schmidt, Peter**; Schmahl, Wolfgang; Scherer, Johanna; Anton-Lamprecht, Ingrun; Von Figura, Kurt; Paus, Ralf; Peters, Christoph
CORPORATE SOURCE: Institut fur Molekulare Medizin und Zellforschung, Albert Ludwigs Universitat Freiburg, Freiburg, 79106, Germany
SOURCE: FASEB Journal (2000), 14(13), 2075-2086
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lysosomal cysteine proteinases of the papain family are involved in lysosomal bulk proteolysis, major histocompatibility complex class II mediated antigen presentation, prohormone processing, and extracellular matrix remodeling. Cathepsin L (CTSL) is a ubiquitously expressed major representative of the papain-like family of cysteine proteinases. To

investigate CTSL in vivo functions, the gene was inactivated by gene targeting in embryonic stem cells. CTSL-deficient mice develop periodic hair loss and epidermal hyperplasia, acanthosis, and hyperkeratosis. The hair loss is due to alterations of hair follicle morphogenesis and cycling, dilatation of hair follicle canals, and disturbed club hair formation. **Hyperproliferation** of hair follicle epithelial cells and basal epidermal keratinocytes-both of ectodermal origin-are the primary characteristics underlying the mutant phenotype. Pathol. inflammatory responses have been excluded as a putative cause of the skin and hair disorder. The phenotype of CTSL-deficient mice is reminiscent of the spontaneous mouse mutant furless (fs). Analyses of the ctsl gene of fs mice revealed a G149R mutation inactivating the proteinase activity. CTSL is the first lysosomal proteinase shown to be essential for epidermal homeostasis and regular hair follicle morphogenesis and cycling.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 16 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:894792 HCAPLUS
DOCUMENT NUMBER: 134:141823
TITLE: New LHRH antagonists with enhanced biological activity: Preclinical and clinical results
AUTHOR(S): Kutscher, Bernhard; Bernd, Michael; **Gunther, Eckhard**; Deger, Wolfgang; Reissmann, Thomas; Beckers, Thomas; Deghenghi, Romano; Engel, Jurgen
CORPORATE SOURCE: Corporate Research, ASTA Medica AG, Frankfurt, D-60314, Germany
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 655-657. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A brief review/discussion with 4 refs. on the title topic with focus on Cetrorelix, Antarelix, and D-26344 and their use in treating sex hormone-dependent **tumors** and nonmalignant conditions.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 17 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:679914 HCAPLUS
DOCUMENT NUMBER: 134:187901
TITLE: In vivo depletion of B cells using a combination of high-dose cytosine arabinoside/mitoxantrone and rituximab for autografting in patients with non-Hodgkin's lymphoma
AUTHOR(S): Voso, Maria Teresa; Pantel, Gitta; Weis, Mirjam; **Schmidt, Petra**; Martin, Simona; Moos, Marion; Ho, Anthony D.; Haas, Rainer; Hohaus, Stefan
CORPORATE SOURCE: Department of Internal Medicine V, University of Heidelberg, Heidelberg, Germany
SOURCE: British Journal of Haematology (2000), 109(4), 729-735
CODEN: BJHEAL; ISSN: 0007-1048
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We performed a pilot study including rituximab (Mabthera: IDEC-C2B8,

Hoffmann-La Roche) with a sequential high-dose therapy protocol in 15 patients with follicular and three patients with mantle cell lymphoma and studied the potential of the chemoimmunotherapy to induce depletion of **malignant** B cells in vivo. Our treatment protocol included induction with three cycles of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) chemotherapy, followed by peripheral blood stem cell (PBSC) mobilization using high-dose cytosine arabinoside (2 g/m2 every 12 h, days 1 and 2) and mitoxantrone (10 mg/m2, days 2 and 3) (HAM), preceded by rituximab (375 mg/m2). The proportion of CD19+ B cells in blood and bone marrow decreased from 1.2 ± 0.4% to 0.13 ± 0.1% (P = 0.01) and from 2.7 ± 0.8% to 0.8 ± 0.5% (P = 0.03) resp. The number of t(14:18)-pos. cells in blood and bone marrow progressively decreased with treatment, as assessed by the quant. real-time PCR assay in four patients. Conversion to PCR-negativity was achieved in the peripheral blood (PB) of seven informative patients. Leucaphereses were performed during the granulocyte colony-stimulating factor (G-CSF)-supported leukocyte recovery phase. In 17 of 18 patients, a median of 15.1 + 106 CD34+ cells/kg body weight (BW) could be harvested by a single procedure for enrichment by an immunomagnetic method. Leucapheresis products contained 51.3 ± 28.8 + 104 CD19+ B cells/kg BW (mean) and were t(14:18) PCR neg. in all seven informative patients. These data compare favorably with results obtained in patients treated with the same regimen without rituximab. The high-dose therapy (n = 12 patients), including total body irradiation (14.4 Gy) and cyclophosphamide (200 mg/kg BW), was also preceded by rituximab. Recovery of neutrophils to > 0.5 + 109/l and of platelets to > 20 + 109/l required a median of 13.5 and 11.5 d (range 11-24 and 9-24 d) resp. In conclusion, the addition of the CD20 antibody to chemotherapy ensured **tumor** depletion in vivo and allowed the collection of PBSCs devoid of **tumor** cells and with conserved engraftment capability.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 18 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:666761 HCAPLUS
DOCUMENT NUMBER: 133:256821
TITLE: Novel LHRH antagonists with improved solubility characteristics
INVENTOR(S): Bernd, Michael; Kutscher, Bernhard; **Gunther, Eckhard**; Romeis, Peter; Reissmann, Thomas; Beckers, Thomas
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000055190	A1	20000921	WO 2000-EP2165	20000311
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19911771	A1	20000928	DE 1999-19911771	19990317
CA 2381461	AA	20000921	CA 2000-2381461	20000311
BR 2000009472	A	20011127	BR 2000-9472	20000311

EP 1163264	A1	20011219	EP 2000-910816	20000311
EP 1163264	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103339	T2	20020422	TR 2001-200103339	20000311
JP 2002543045	T2	20021217	JP 2000-605616	20000311
AU 759442	B2	20030417	AU 2000-32887	20000311
NZ 514830	A	20030530	NZ 2000-514830	20000311
RU 2227145	C2	20040420	RU 2001-128232	20000311
AT 277077	E	20041015	AT 2000-910816	20000311
ES 2225103	T3	20050316	ES 2000-910816	20000311
NO 2001004486	A	20011102	NO 2001-4486	20010914
ZA 2001007753	A	20020513	ZA 2001-7753	20010919
BG 106008	A	20020628	BG 2001-106008	20011011
HK 1045531	A1	20050520	HK 2002-107028	20020926
US 2004266695	A1	20041230	US 2003-671573	20030929
PRIORITY APPLN. INFO.:			DE 1999-19911771	A 19990317
			WO 2000-EP2165	W 20000311
			US 2000-525007	A3 20000314

OTHER SOURCE(S): MARPAT 133:256821

AB The invention relates to peptides which contain N-methylated amino acid building blocks and are provided with improved water solubility Medicaments containing the inventive peptides can be used for the treatment of hormone-dependent **tumors** and hormone-influenced, non-**malignant** diseases.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 19 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:241650 HCAPLUS

DOCUMENT NUMBER: 132:248282

TITLE: Screen for risk for gastric adenocarcinoma

INVENTOR(S): Goldenring, James R.; **Schmidt, P. Henry**; Lee, Jeffrey R.

PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, USA

SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020868	A1	20000413	WO 1998-US20820	19981001
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2345663	AA	20000413	CA 1998-2345663	19981001
AU 9896810	A1	20000426	AU 1998-96810	19981001
AU 765082	B2	20030911		
EP 1121597	A1	20010808	EP 1998-950883	19981001
R: CH, DE, FR, GB, IT, LI				
JP 2002526776	T2	20020820	JP 2000-574935	19981001
PRIORITY APPLN. INFO.:			WO 1998-US20820	A 19981001

AB It has been determined that a specific metaplastic lineage that contains immunoreactivity for a trefoil polypeptide, spasmolytic peptide, is associated with and gives rise to the vast majority of human adenocarcinomas. The identification of this Spasmolytic Polypeptide Expressing Metaplasia (SPEM) is a major factor for grading of biopsies of the stomach to assess

risk for gastric **cancer.** It also forms the basis of a method for serol. screening for those at risk for gastric **cancer.** In a preferred embodiment, antibodies to spasmolytic peptide (hSP) are used in immunostaining of biopsies of gastric tissue obtained by endoscopy for grading biopsies. Those patients having these cells, characterized by a morphol. more typical of a type of cell present normally in the intestine and not stomach, Brunner's gland cells, are at risk of developing adenocarcinoma. Since these cells express hSP, antibodies or nucleic acid probes hybridizing to mRNA encoding hSP, can be used for rapid detection of the cells in tissue biopsies. The antibodies can also be used in serol. tests for screening and following patients at risk for gastric **cancer.** In combination with evidence of previous or present infection with H. pylori, the test are predictive of the likelihood of developing adenocarcinoma.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 20 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:177658 HCAPLUS
DOCUMENT NUMBER: 132:274157
TITLE: Thiazolidinedione-induced activation of the transcription factor peroxisome **proliferator** -activated receptor γ in cells adjacent to the murine skeletal muscle: implications for fibroblast functions
AUTHOR(S): Lohrke, B.; Shahi, S. K.; Kruger, B.; **Schmidt, P.**; Renne, U.; Dietl, G.
CORPORATE SOURCE: Research Institute of Animal Biology, Dummerstorf, D-18196, Germany
SOURCE: Pfluegers Archiv (2000), 439(3), 288-296
CODEN: PFLABK; ISSN: 0031-6768
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Nuclear peroxisome **proliferator**-activated receptor γ (PPARγ) is the target of antidiabetogenic thiazolidinediones (TZD). However, recent studies failed to show that TZD has an effect in vitro on insulin-regulated glucose uptake in skeletal muscles, the major site of glucose disposal. The potential effects of TZD on cells adjacent to skeletal muscles are not well characterized but may be involved in TZD's actions. Hence, we studied these cells from mice treated with the carrier and with the TZD ciglitazone (9 nmol/g body weight). The cells were typified by lipid enrichment (floating adipocytes and macrophages), by the ectopic expression of cellular fibronectin (fibroblasts), fibronectin and PPARγ (preadipocytes), PPARγ and CD11b/Mac-1 (active macrophages) as revealed by flow cytometry and immunoblotting. The glucose transporter 4 proteins (GLUT4) and the uptake of glucose and long-chain fatty acids (LCFA) were determined flow cytometrically using fluorescent derivs. of glucose (NBDG) and LCFA (C16-Bodipy). The expression of **tumor** necrosis factor α (TNFα) in CD11b/Mac-1-pos. and CD11b/Mac-1-neg. cells separated by magnetic immunobeads was analyzed. The results showed that TZD treatment upregulated GLUT4 expression, and increased insulin-regulated NBDG uptake and C16-Bodipy binding and influx, at the same time as increasing the quantity of PPARγ-expressing fibroblasts; this indicates the development of the preadipocyte phenotype. In contrast, TZD lowered the number of adipocytes (0.6-fold compared to the carrier-treated control) perhaps through an action of TNFα from CD11b- and PPARγ-expressing macrophages. The data suggest that the regulatory effects of TZD on energy homeostasis involve two major targets: the PPARγ-pos. fibroblasts whose

adipogenic program is promoted, and CD11b-PPARγ-expressing macrophages which become cytotoxic and fibrogenic because of the effects of TNFα on neighboring adipocytes and fibroblasts, resp.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 21 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:146227 HCAPLUS
DOCUMENT NUMBER: 132:292678
TITLE: Heat shock protein 70 is able to prevent heat shock-induced resistance of target cells to CTL
AUTHOR(S): Dressel, Ralf; Elsner, Leslie; Quentin, Thomas; Walter, Lutz; **Gunther, Eberhard**
CORPORATE SOURCE: Division of Immunogenetics, University of Gottingen, Gottingen, D-37073, Germany
SOURCE: Journal of Immunology (2000), 164(5), 2362-2371
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heat shock or transfection with heat shock protein 70 (Hsp70) genes has been shown to protect **tumor** cell lines against immune mechanisms of cytotoxicity. The authors have reported previously that heat shock confers resistance to CTL in the rat myeloma cell line Y3 that is Hsp70 defective. Evidence is now presented that Hsp70 is able to prevent the induction of the resistant phenotype. In Con A-stimulated lymphocytes and in lymphocyte + Y3 somatic cell hybrid clones a severe, non-Hsp70-inducing heat shock elicits resistance to CTL in contrast to a heat shock that results in Hsp70 expression. Thus, Hsp70 expression appears to be neg. associated with the development of resistance. Furthermore, loading of Y3 cells with recombinant Hsp70 protein before heat shock is able to prevent resistance. Because apoptosis induced in Y3 cells by heat shock is not affected, Hsp70 appears to interfere selectively with the CTL-induced lethal pathway that is calcium but not caspase dependent. It is suggested that after heat shock Hsp70 enhances the CTL-induced apoptotic pathway by chaperoning certain proteins in the target cell that are involved in the execution of cell death. Thus, although shown to confer protection against many cytotoxic mechanisms, Hsp70 does not appear to be generally cytoprotective. This observation could also be of relevance when interpreting the effectiveness of **tumor** immunity.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 22 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:602212 HCAPLUS
DOCUMENT NUMBER: 131:285206
TITLE: Suppression of interleukin-12 production by human monocytes after preincubation with lipopolysaccharide
AUTHOR(S): Wittmann, Miriam; Larsson, Vivi-Ann; **Schmidt, Petra**; Begemann, Gabriele; Kapp, Alexander; Werfel, Thomas
CORPORATE SOURCE: Department of Dermatology and Allergology, Hannover Medical University, Hannover, D-30449, Germany
SOURCE: Blood (1999), 94(5), 1717-1726
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin-12 (IL-12) is a potent proinflammatory and immunoregulatory

cytokine skewing T lymphocytes to express a type 1 cytokine pattern. Optimal expression of IL-12 mRNA and bioactivity in vitro requires specific priming of monocytes by interferon-γ (IFN-γ) or granulocyte-macrophage colony-stimulating factor (GM-CSF) before lipopolysaccharide (LPS) stimulation. We show here for the first time that the production of IL-12 by IFN-γ- or GM-CSF-primed human monocytes can be completely suppressed by preincubation with LPS (from Escherichia coli Serotype 055:B5) for 6 to 24 h before the priming procedure. A dose-dependent suppression of IL-12p70 was measured on the levels of intracellular cytokine production and cytokine secretion. MRNA studies on the expression of p40 and p35 showed an LPS-induced downregulation of both subunits. The results of several different exptl. approaches suggest that IL-12 downregulation was not due to endogenous IL-10, IL-4, prostaglandin E2 (PGE2), **tumor** necrosis factor-α (TNF-α), or nitric oxide (NO) production induced by LPS. Moreover, preincubation of monocytes with LPS did not lead to a downregulation of the CD14 antigen, which is an LPS receptor. LPS preincubation in this exptl. setting did not result in a general hyporesponsiveness of the monocytes, as IL-6 production as well as IFN-γ-induced upregulation of CD54 did not decline. Downregulation of IL-12 was not due to changes in mRNA stability. These findings show that the immunoregulatory important cytokine, IL-12, underlies itself a complex regulation.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 23 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:587287 HCAPLUS

DOCUMENT NUMBER: 131:266704

TITLE: **Anticancer** drug sensitivity and expression of multidrug resistance markers in early passage human sarcomas

AUTHOR(S): Hoffmann, Jens; **Schmidt-Peter, Peter**; Hansch, Wolfgang; Naundorf, Helga; Bunge, Andreas; Becker, Michael; Fichtner, Iduna

CORPORATE SOURCE: Max-Delbruck-Center of Molecular Medicine, Berlin, 13122, Germany

SOURCE: Clinical Cancer Research (1999), 5(8), 2198-2204
CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

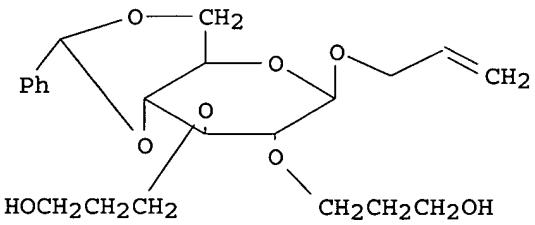
LANGUAGE: English

AB We have established new human sarcoma lines and examined their sensitivity to common **antitumor** drugs and expression of putative multidrug resistance (MDR) proteins. Eighty-two sarcoma samples were transplanted in nude mice. Fourteen of these sarcomas were established as **tumor** cell lines. We determined a chemosensitivity profile to **antitumor** drugs (MDR drugs = doxorubicin, mitoxantrone, and vincristine; non-MDR drugs = cisplatin, ifosfamide, and bleomycin) for each **tumor** line in vivo. Response to chemotherapy with doxorubicin and ifosfamide was observed in 30-50% of these **tumor** lines. Our results obtained with xenotransplants are similar to the results documented in clin. trials in which doxorubicin and ifosfamide are effective in 30-50% of the patients. Furthermore, we examined expression of MDR-relevant markers like P-glycoprotein, MDR-associated protein, lung resistance protein, and mdr1 mRNA in these xenotransplants. A relationship between mdr1 mRNA expression and response to doxorubicin was demonstrated in >90% of our **tumor** lines. In six sarcomas with mdr1 mRNA expression, five were resistant against doxorubicin and cross-resistant against several other drugs, whereas from eight sarcomas, which lacked detectable mdr1 mRNA, seven were sensitive to doxorubicin and

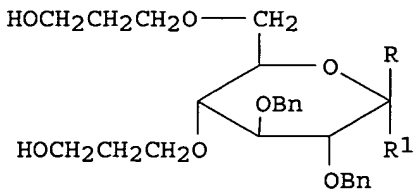
other drugs. We found lung resistance protein or MDR-associated protein expressed in three resistant and mdr1 mRNA-pos. sarcomas. These results demonstrate that mdr1 mRNA expression is a putative marker for drug resistance in our sarcoma lines. We conclude, therefore, that inherent P-glycoprotein expression might be also responsible for drug resistance occurring in treatment of patients with sarcomas. The established **tumor** lines are useful for addnl. investigations on mechanisms of drug resistance in sarcomas and as models for preclin. screening of new **antitumor** drugs.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 24 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:572216 HCAPLUS
DOCUMENT NUMBER: 131:272102
TITLE: A practical synthesis of benzyl α- and allyl β-D-glucopyranosides regioselectively substituted with (CH2)3OH groups. Stereocontrolled β-galactosidation by cation π-interaction
AUTHOR(S): Neda, Ion; Sakhaii, Peyman; Wassmann, Anke; Niemeyer, Ulf; **Gunther, Eckhard**; Engel, Jurgen
CORPORATE SOURCE: Institut Anorganische Analytische Chemie, Technische Univ. Braunschweig, Braunschweig, D-38023, Germany
SOURCE: Synthesis (1999), (9), 1625-1632
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:272102
GI



I



II

AB Efficient synthesis of the 2,3- or 4,6-di-O-hydroxypropyl-functionalized glucose derivs. I and II (R = allyloxy, R1 = H; R = H, R1 = PhCH2O) is presented. These compds. represent potential precursors for the synthesis

of multi-antennary oligosaccharides. A new method was developed for the β-stereoselective galactosylation using galactosyl difluorophosphate as galactosyl donor and tetra-O-propylated cone-calix[4]arene as stabilizer for the oxo-carbenium ion. The latter compound is intended to serve (via immobilization on solid phase and subsequent deprotection) as affinity ligand in the isolation of **tumor** cell lectins via affinity chromatog.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 25 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:506689 HCAPLUS
DOCUMENT NUMBER: 131:164822
TITLE: DaunoXome (liposomal daunorubicin) for first-line treatment of advanced, HIV-related Kaposi's sarcoma
AUTHOR(S): Mukwaya, Geoffrey; Forssen, Eric A.; **Schmidt, Paul**; Ross, Michael
CORPORATE SOURCE: NeXstar Pharmaceuticals, San Dimas, CA, USA
SOURCE: Long Circulating Liposomes (1998), 147-163. Editor(s): Woodle, Martin C.; Storm, Gerrit. Springer: Berlin, Germany. CODEN: 67YZAE
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 47 refs. This chapter reviews the chemical, clin. pharmacokinetics, efficacy, safety and tolerability of DaunoXome (daunorubicin citrate liposome injection). DaunoXome represents a significant advance in drug delivery for the selective targeting of **tumor** cells and offers a new first-line treatment option for advanced, HIV-associated Kaposi's sarcoma.
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 26 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:340306 HCAPLUS
DOCUMENT NUMBER: 131:153872
TITLE: Induction of the PAC1-R (PACAP-type I receptor) gene by p53 and Zac
AUTHOR(S): Ciani, Elisabetta; Hoffmann, Anke; **Schmidt, Peer**; Journot, Laurent; Spengler, Dietmar
CORPORATE SOURCE: Department of Molecular Neurobiology, Max Planck Institute of Psychiatry, Munich, D-80804, Germany
SOURCE: Molecular Brain Research (1999), 69(2), 290-294 CODEN: MBREE4; ISSN: 0169-328X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Pituitary adenylate cyclase-activating polypeptides and PAC1-R are expressed during early embryogenesis and PACAP's neurotrophic action supports a role in neuronal development. In the adult brain PACAP functions as a neuroprotective factor that attenuates the neuronal damage resulting from various insults. The **tumor** suppressor gene p53 and the new zinc finger protein Zac regulate apoptosis and cell cycle arrest through unrelated pathways and both genes are up-regulated under cerebral ischemia. We report here that p53 and Zac induce expression of the PAC1-R gene. By this mechanism p53 and Zac could fine-tune the balance between death promoting and protective signals and may thus fulfill a dual role in ischemia.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 27 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:321121 HCAPLUS
DOCUMENT NUMBER: 131:87336
TITLE: Docosahexaenoic acid ingestion inhibits natural killer cell activity and production of inflammatory mediators in young healthy men
AUTHOR(S): Kelley, D. S.; Taylor, P. C.; Nelson, G. J.; **Schmidt, Perla C.**; Ferretti, Aldo; Erickson, Kent L.; Yu, Rina; Chandra, Ranjit K.; Mackey, B. E.
CORPORATE SOURCE: USDA, ARS, Western Human Nutrition Research Center, Presidio of San Francisco, CA, 94129, USA
SOURCE: Lipids (1999), 34(4), 317-324
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of dietary docosahexaenoic acid (DHA) as triacylglycerol on the fatty acid composition, eicosanoid production, and some activities of human peripheral blood mononuclear cells (PBMNC) were studied for 120 days in 11 healthy men. Four subjects (controls) were fed the stabilization diet throughout the study; the remaining 7 subjects were fed the basal diet for the first 30 days, followed by 6 g DHA/day for 90 days. DHA replaced an equivalent amount of linoleic acid; the 2 diets were comparable in their total fat and other nutrients. Both diets were supplemented with 20 mg D-α-tocopherol acetate per day. PBMNC fatty acid composition and eicosanoid production were examined on days 30 and 113; immune cell functions were tested on days 22, 30, 78, 85, 106, and 113. DHA increased its concns. from 2.3 to 7.4 wt% in the PBMNC total lipids and decreased the arachidonic acid concns. from 19.8 to 10.7 wt%. It also lowered the PGE2 and LTB4 production by 60-75% in response to lipopolysaccharide. The natural killer cell activity and in vitro secretion of interleukin-1β and **tumor** necrosis factor-α were decreased by DHA. These parameters remained unchanged in the control subjects. B-cell functions reported here and T-cell functions reported previously were not altered by DHA. The blood serum levels of antioxidant vitamins (retinol, β-carotene, α-tocopherol, ascorbic acid) were not affected by the DHA intake. Thus, inhibitory effects of DHA on immune cell functions varied with the cell type and the inhibitory effects were not mediated by increased production of PGE2 and LTB4.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 28 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:244571 HCAPLUS
DOCUMENT NUMBER: 130:276778
TITLE: Methods of modulating serine/threonine protein kinase function with 5-azaquinoxaline-based compounds, compound preparation, and therapeutic use
INVENTOR(S): McMahon, Gerald; Kutscher, Bernhard; **Gunther, Eckhard**; App, Harald
PATENT ASSIGNEE(S): Asta Medica A.-G., Germany
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9917759	A2	19990415	WO 1998-US20910	19981005
WO 9917759	A3	20000106		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9808961	A	19991004	ZA 1998-8961	19981001
CA 2306257	AA	19990415	CA 1998-2306257	19981005
AU 9895141	A1	19990427	AU 1998-95141	19981005
AU 757585	B2	20030227		
EP 1028729	A2	20000823	EP 1998-948606	19981005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO				
BR 9814814	A	20001003	BR 1998-14814	19981005
TR 200000906	T2	20001121	TR 2000-200000906	19981005
US 6180631	B1	20010130	US 1998-166723	19981005
JP 2001518496	T2	20011016	JP 2000-514630	19981005
TR 200100385	T2	20020621	TR 2001-200100385	19981005
NZ 503431	A	20020726	NZ 1998-503431	19981005
RU 2223753	C2	20040220	RU 2000-111434	19981005
MX 200003255	A	20001110	MX 2000-3255	20000403
NO 2000001748	A	20000405	NO 2000-1748	20000405
BG 104392	A	20001229	BG 2000-104392	20000428
US 6727252	B1	20040427	US 2000-688199	20001016
HK 1031836	A1	20050401	HK 2001-102529	20010410
PRIORITY APPLN. INFO.:			US 1997-61123P P	19971006
			US 1998-166723 A3	19981005
			WO 1998-US20910 W	19981005

OTHER SOURCE(S): MARPAT 130:276778

AB Methods are provided for modulating the function of serine/threonine protein kinases with 5-azaquinoxaline-based compds. The methods incorporate cells that express a serine/threonine protein kinase, e.g. RAF. In addition,methods are described for preventing and treating serine/threonine protein kinase-related abnormal conditions (e.g. **cancer**) in organisms with a compound identified by the invention. Furthermore, the invention pertains to 5-azaquinoxaline compds., their preparation, and pharmaceutical compns. comprising them.

L41 ANSWER 29 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:214870 HCAPLUS

DOCUMENT NUMBER: 131:1090

TITLE: Postnatal overexpression of insulin-like growth factor II in transgenic mice is associated with adrenocortical hyperplasia and enhanced steroidogenesis

AUTHOR(S): Weber, Matthias M.; Fottner, Christian; **Schmidt, Peter**; Brodowski, Kathrin M. H.; Gittner, Katinka; Lahm, Harald; Engelhardt, Dieter; Wolf, Eckhard

CORPORATE SOURCE: Medical Department II, Laboratory of Endocrine Research, Klinikum Grosshadern, Munich, 81377, Germany

SOURCE: Endocrinology (1999), 140(4), 1537-1543
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The influence of postnatal insulin-like growth factor II (IGF-II) overexpression on adrenal growth and function was investigated in 3-mo-old male phosphoenolpyruvate carboxykinase (PEPCK) promoter human IGF-II transgenic mice, which are characterized by 4-to 6-fold elevated postnatal IGF-II serum levels. Plasma corticosterone levels of PEPCK-IGF-II transgenic mice were 2-fold higher than in age- and sex-matched controls, both in the morning (7.4 vs. 17.8 ng/mL) and in the evening (33.3 vs. 65.3 ng/mL). When PEPCK-IGF-II transgenic mice were subjected to an ACTH challenge, corticosterone levels were stimulated 6-fold, to 396 ng/mL after 60 min, compared with 230 ng/mL in the control group. In contrast to corticosterone, plasma ACTH levels were similar in transgenic and control mice, excluding an indirect effect of IGF-II at the hypothalamic or pituitary level. In vitro, the basal and ACTH-induced corticosterone production of adrenal glands from transgenic mice was higher (2-fold and 1.8-fold, resp.) than that of control organs. However, when normalized for adrenal weight, the in vitro corticosterone secretion was similar in both groups. At autopsy, adrenal wts. of transgenic mice were significantly greater than those of control adrenal glands (3.3 vs. 2.0 mg). Furthermore, a local expression of human IGF-II could be demonstrated in transgenic adrenal glands by RT-PCR, whereas in normal adult mice, no adrenal expression of IGF-II was detected. Stereol. investigation of adrenal glands from another set of PEPCK-IGF-II transgenic mice and controls (6-mo-old males) demonstrated that the increase in adrenal weight in transgenic mice is mainly caused by a 50% increase in the number of zona fasciculata cells, whereas cell volume and zonation of transgenic adrenal glands remained unchanged. In conclusion, the authors' data indicate that postnatal overexpression of IGF-II induces an increased adrenal weight and elevated corticosterone serum levels, presumably by a direct mitogenic effect of IGF-II on adrenocortical fasciculata cells.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 30 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:203983 HCAPLUS

DOCUMENT NUMBER: 131:42640

TITLE: PlAP as a marker for germ cell **tumors**

AUTHOR(S): Albrecht, Walter; Bonner, Elisabeth; Jeschke, Klaus; Stoiber, Franz; **Schmidt, Peter**; Scheiber, Karl; Kozak, Walter; De Santis, Maria; Schwarzmaier, Alexandra

CORPORATE SOURCE: Department of Urology, Rudolfstiftung, Vienna, A-1030, Austria

SOURCE: Germ Cell Tumours IV, Proceedings of the Germ Cell Tumour Conference, 4th, Leeds, UK, Nov. 13-16, 1997 (1998), Meeting Date 1997, 105-109. Editor(s): Jones, W. G. Libbey: London, UK.
CODEN: 67LZAH

DOCUMENT TYPE: Conference; General Review

LANGUAGE: English

AB A review, with 16 refs. To determine the usefulness of placental alkaline phosphatase (PlAP) as a marker for germ cell **tumors** the current literature has been reviewed and the preliminary results of a retrospective anal., currently performed by the Austrian Uro-Oncol. Group, are reported. PlAP is an excellent tissue marker for seminoma and for intraepithelial **neoplasia** (TIN) in biopsies of the testis. Irresp. of the **tumor** stage, PlAP serum assays were pos. in 72% of seminoma patients. In 21% of cases PlAP was the only pos. marker. Combining PlAP with HCG and LDH gave a marker incidence in seminomas comparable to that in non-seminomatous **tumors.** There is strong

evidence that seminomatous elements and surrounding TIN in the primary **tumor** are responsible for the 36% PlAP positivity in non-smoking NSGCT patients. Serum PlAP half-life in non-smokers was calculated to be 0.4-2.8 days. Prolonged half-life correlated well with known higher stages and therefore may be also able to identify patients with clin. undetectable metastases. PlAP decline during chemotherapy of higher stages correlated very well with clin. response. During follow-up the false pos. rate in non-smokers in stage I disease was no more than 3% vs. 38% in smokers. In all but one non-smoker, disease progression was associated with PlAP levels above 100 U/L. Determination of PlAP levels should be mandatory in non-smokers with seminoma, but as PlAP levels vary too much due to smoking, they should not be performed routinely in smokers.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 31 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:92983 HCAPLUS
TITLE: Application of aptamers in functional nuclear imaging
AUTHOR(S): Stephens, A. W.; Hicke, B. J.; McBride, B. C.; Chang, Y-F.; **Schmidt, P. G.**; Dinkelborg, L.; Hilger, C. S.
CORPORATE SOURCE: NeXstar Phamaceuticals Inc., Boulder, CO, 80301, USA
SOURCE: Book of Abstracts, 217th ACS National Meeting, Anaheim, Calif., March 21-25 (1999), NUCL-186. American Chemical Society: Washington, D. C.
CODEN: 67GHA6
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB Aptamers represent a new class of imaging reagents, characterized by high binding affinity and specificity, low mol. weight, and rapid blood clearance. Nucleic acid aptamers have been used to image vascular and **tumor** targets in animal models by gamma scintigraphy. Aptamers are selected from large nuclease-resistant oligonucleotide libraries (10e14 sequences) by SELEX (Systematic Evolution of Ligands by EXponential enrichment). Selected aptamers have a high affinity for their target (Kd .apprx. 0.1-10 nM). Oligonucleotides produced transcriptionally or synthetically can be conjugated to Tc-99m chelate moieties, retaining their binding affinity, and labeling to specific activities of 3,000 MBq/mg. Tc-99m-labeled aptamers are able to bind their resp. targets in vivo. Biodistribution studies indicate target to blood ratios of 30-65 within 4 h. Examples of thrombus and **tumor** imaging will be presented.

L41 ANSWER 32 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:64168 HCAPLUS
DOCUMENT NUMBER: 130:279968
TITLE: Heterogeneous patterns of constitutive and heat shock induced expression of HLA-linked HSP70-1 and HSP70-2 heat shock genes in human melanoma cell lines
AUTHOR(S): Dressel, R.; Johnson, J. P.; **Gunther, E.**
CORPORATE SOURCE: Division of Immunogenetics, University of Gottingen, Gottingen, D-37073, Germany
SOURCE: Melanoma Research (1998), 8(6), 482-492
CODEN: MREEEH; ISSN: 0960-8931
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The heat shock response, which is characterized by the induction of heat shock proteins, is known to affect the ability of **tumor** cells to cope with potentially adverse conditions such as hypoxia, glucose

starvation and cytotoxic immune reactions. To assess the heat shock response of melanoma cells, spontaneous and heat shock induced expression of heat shock proteins was analyzed in a panel of 17 human melanoma cell lines. Constitutive expression of HSP27, HSP70, HSC70, HSP90αβ and GRP94 proteins was found in all the melanoma cell lines, and HSP70 and HSC70 were also induced by heat shock. The major heat inducible HLA-linked HSP70-1 and HSP70-2 genes were analyzed at the mRNA level. Basal expression and inducibility varied between the different melanoma cell lines. In addition, in situ hybridization demonstrated heterogeneous expression of these genes among single cells of a given cell line. In general, each melanoma cell line appears to exhibit an individual type of HSP70 expression that might reflect selection during **tumor** progression and therapy.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 33 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:45206 HCAPLUS
DOCUMENT NUMBER: 130:105314
TITLE: Vascular endothelial growth factor nucleic acid ligand complexes with lipophilic compounds
INVENTOR(S): Janjic, Nebojsa; Gold, Larry; **Schmidt, Paul**
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: U.S., 26 pp., Cont.-in-part of U.S. Ser. No. 434,465.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859228	A	19990112	US 1996-739109	19961025
US 6011020	A	20000104	US 1995-434465	19950504
CA 2269072	AA	19980507	CA 1997-2269072	19971017
WO 9818480	A1	19980507	WO 1997-US18944	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, MZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9749904	A1	19980522	AU 1997-49904	19971017
AU 733674	B2	20010524		
EP 957929	A1	19991124	EP 1997-912811	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 334859	A	20010223	NZ 1997-334859	19971017
JP 2001505191	T2	20010417	JP 1998-520553	19971017
JP 3626503	B2	20050309		
RU 2177950	C2	20020110	RU 1999-110377	19971017
KR 2000052697	A	20000825	KR 1999-703488	19990421
AU 773741	B2	20040603	AU 2001-18257	20010202
AU 773815	B2	20040610	AU 2001-29834	20010323
US 2003114404	A1	20030619	US 2002-205009	20020725
US 2004192632	A1	20040930	US 2004-832941	20040426
JP 2005046160	A2	20050224	JP 2004-301813	20041015

PRIORITY APPLN. INFO.: US 1995-434465 A2 19950504

US 1990-536428	B2	19900611
AU 1991-82061	A0	19910610
US 1991-714131	A2	19910610
US 1994-234997	A2	19940428
AU 1996-58839	A3	19960530
AU 1996-61611	A3	19960604
US 1996-739109	A	19961025
US 1997-870930	A	19970606
US 1997-897341	A	19970721
US 1997-897351	A	19970721
JP 1998-520553	A3	19971017
WO 1997-US18944	W	19971017
US 2000-254968	A3	20000313
US 2002-205009	A1	20020725

AB This invention discloses a method for preparing a complex comprised of a vascular endothelial growth factor (VEGF) nucleic acid ligand and a lipophilic compound by identifying a VEGF nucleic acid ligand by SELEX (systematic evolution of ligands by exponential enrichment) methodol. and associating the VEGF nucleic acid ligand with a non-immunogenic lipophilic compound The invention further discloses complexes comprising one or more VEGF nucleic acid ligands in association with a lipophilic compound Thus, two of these products were tested for their ability to form covalent-bonded complexes with VEGF165 and, in the form of liposomes, showed biol. activity in human umbilical vein endothelial cell **proliferation**, angiogenesis (using chicken allantoic membrane), and as **antitumor** agents against Kaposi's sarcoma cell lines in vitro.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 34 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:628382 HCAPLUS
DOCUMENT NUMBER: 130:945
TITLE: Reduced susceptibility of electroporated **tumor** cell lines to killing by cytotoxic lymphocytes
AUTHOR(S): Dressel, Ralf; Baraki, Husnia; Langer, Frank; **Gunther, Eberhard**
CORPORATE SOURCE: Divisions of Immunogenetics, University of Gottingen, Gottingen, D-37073, Germany
SOURCE: Biochemical and Biophysical Research Communications (1998), 250(2), 259-263
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Electroporation is a widely applied method for gene or protein transfer into cells, and it is also used for electrochemotherapy of **cancer** . During gene transfection studies, electroporation was found to decrease transiently susceptibility of some **tumor** cell lines to alloreactive cytotoxic T lymphocytes (CTL) or lymphokine-activated killer cell (LAK) cells. In each cell line electroporation induced c-fos mRNA. In K562 cells HSP70 mRNA induction also occurred. Expression of Grp78, Bcl-2, CD95/Fas, or major histocompatibility complex class I mols. was not affected by electroporation. (c) 1998 Academic Press.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 35 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:626255 HCAPLUS
DOCUMENT NUMBER: 130:35089
TITLE: 188Re DD-3B6/22 Fab' for use in therapy of ovarian

cancer: labeling and animal studies
AUTHOR(S): **Schmidt, Peter F.**; Smith, Suzanne V.; Bundesen, Peter G.
CORPORATE SOURCE: Radiopharmaceutical Division Research and Development, Australian Nuclear Science and Technology Organisation (ANSTO), Menai, 2234, Australia
SOURCE: Nuclear Medicine and Biology (1998), 25(7), 639-649
CODEN: NMBIEO; ISSN: 0969-8051
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A fast and high yielding method of 188Re radiolabelling DD-3B6/22 Fab' is described. An inert atmospheric [N2(g)] and ascorbic acid was essential for preparation and storage of therapeutic levels (≤2 GBq/mg) for up to 24 h. Immunoreactivity was greater than 75%. Pharmacokinetic studies in nu/nu mice demonstrated localisation of 188Re DD-3B6/22 Fab' was equivalent and correlated well with the behavior observed for 99mTc DD-3B6/22 Fab' used to image ovarian **cancer.** Excellent stability at the target site in vivo supports the potential use of 188Re DD-3B6/22 Fab' in the therapy of ovarian **cancer.**
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 36 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:293387 HCAPLUS
DOCUMENT NUMBER: 129:16346
TITLE: Synthesis of nucleic acids and preparation of vascular endothelial growth factor (vegf) nucleic acid ligand complexes
INVENTOR(S): Janjic, Nebojsa; Gold, Larry; **Schmidt, Paul G.**; Vargeese, Chandra; Willis, Michael
PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 127
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818480	A1	19980507	WO 1997-US18944	19971017
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, MZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5859228	A	19990112	US 1996-739109	19961025
US 6168778	B1	20010102	US 1997-870930	19970606
US 6051698	A	20000418	US 1997-897351	19970721
CA 2269072	AA	19980507	CA 1997-2269072	19971017
AU 9749904	A1	19980522	AU 1997-49904	19971017
AU 733674	B2	20010524		
EP 957929	A1	19991124	EP 1997-912811	19971017
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NZ 334859	A	20010223	NZ 1997-334859	19971017

JP 2001505191	T2	20010417	JP 1998-520553	19971017
JP 3626503	B2	20050309		
RU 2177950	C2	20020110	RU 1999-110377	19971017
US 6426335	B1	20020730	US 2000-254968	20000313
AU 773741	B2	20040603	AU 2001-18257	20010202
AU 773815	B2	20040610	AU 2001-29834	20010323
US 2003114404	A1	20030619	US 2002-205009	20020725
US 2004192632	A1	20040930	US 2004-832941	20040426

PRIORITY APPLN. INFO.:

US 1996-739109	A	19961025
US 1997-870930	A	19970606
US 1997-897341	A	19970721
US 1997-897351	A	19970721
US 1990-536428	B2	19900611
AU 1991-82061	A0	19910610
US 1991-714131	A2	19910610
US 1992-964624	A2	19921021
US 1994-233012	A2	19940425
US 1994-234997	A2	19940428
US 1995-434465	A2	19950504
US 1995-447169	A2	19950519
AU 1996-58839	A3	19960530
AU 1996-61611	A3	19960604
WO 1997-US18944	W	19971017
US 2000-254968	A3	20000313
US 2002-205009	A1	20020725

AB This invention discloses a method for preparing a complex comprised of a VEGF (vascular endothelial growth factor) nucleic acid ligand and a non-immunogenic, high mol. weight compound or lipophilic compound by identifying a VEGF nucleic acid ligand by SELEX methodol. and associating the VEGF nucleic acid ligand with a non-immunogenic, high mol. weight compound or lipophilic compound The invention further discloses complexes comprising one or more VEGF nucleic acid ligands in association with a non-immunogenic, high mol. weight compound or lipophilic compound The invention further includes a lipid construct comprising a VEGF nucleic acid ligand or complex and methods for making the same. Thus, a variety of nucleotide-lipid, -phospholipid, or lipid-amides containing 2'-deoxy-2'F-cytidine or -uridine components, and products tested for their ability to form covalent-bonded complexes with VEGF165 ; several of these complexes, some in the form of liposomes, showed biol. activity in human umbilical vein endothelial cell **proliferation**, angiogenesis (using chicken allantoic membrane), and as anti-**tumor** agents against Kaposi's sarcoma cell lines in vitro.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 37 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:129233 HCAPLUS
DOCUMENT NUMBER: 128:255763
TITLE: Membrane potassium channels and human bladder **tumor** cells. I. Electrical properties
AUTHOR(S): Monen, S. H.; **Schmidt, P. H.**; Wondergem, R.
CORPORATE SOURCE: Department of Physiology, James H. Quillen College of Medicine, East Tennessee State University, Johnson City, TN, 37614-0576, USA
SOURCE: Journal of Membrane Biology (1998), 161(3), 247-256
CODEN: JMBBBO; ISSN: 0022-2631
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal

LANGUAGE: English

AB These expts. were conducted to determine the membrane K+ currents and channels in human urinary bladder (HTB-9) carcinoma cells in vitro. K+ currents and channel activity were assessed by the whole-cell voltage clamp and by either inside-out or outside-out patch clamp recordings. Cell depolarization resulted in activation of a Ca2+-dependent outward K+ current, 0.57 nS/pF at -70 mV holding potential and 3.10 nS/pF at 30 mV holding potential. Corresponding patch clamp measurements demonstrated a Ca2+-activated, voltage-dependent K+ channel (KCa) of 214 pS. Scorpion venom peptides, charybdotoxin (ChTx) and iberiotoxin (IbTx), inhibited both the activated current and the KCa activity. In addition, on-cell patch recordings demonstrated an inwardly rectifying K+ channel, 21 pS at pos. transmembrane potential (Vm) and 145 pS at neg. Vm. Glibenclamide (50 μM), Ba2+ (1 mM) and quinine (100 μM) each inhibited the corresponding nonactivated, basal whole-cell current. Moreover, glibenclamide inhibited K+ channels in inside/out patches in a dose-dependent manner, and the IC50 = 46 μM. The identity of this K+ channel with an ATP-sensitive K+ channel (KATP) was confirmed by its inhibition with ATP (2 mM) and by its activation with diazoxide (100 μM). We conclude that plasma membranes of HTB-9 cells contain the KCa and a lower conductance K+ channel with properties consistent with a sulfonylurea receptor-linked KATP.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 38 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:476277 HCAPLUS

DOCUMENT NUMBER: 127:113359

TITLE: Methods for optimizing multicomponent formulations

INVENTOR(S): **Schmidt, Paul**

PATENT ASSIGNEE(S): Nexstar Pharmaceuticals, Inc., USA; Schmidt, Paul

SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9720076	A1	19970605	WO 1996-US19030		19961127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9710852	A1	19970619	AU 1997-10852		19961127
PRIORITY APPLN. INFO.:			US 1995-7694P	P	19951129
			WO 1996-US19030	W	19961127

AB Multicomponent formulations, e.g. drug carriers, are optimized by simultaneous anal. of a large number of mixts. to determine the formulation(s) with optimal properties. The properties to be optimized may be e.g. targeting to **tumor** tissue or a site of infection, optical absorbance, or phys. state (clear solution vs. precipitate). A unique identification marker, capable of being accurately analyzed with higher sensitivity than the formulation itself, is associated with each mixture The optimal formulation is identified by anal. of the marker, which is

specific for a particular set and ratio of ingredients. Preferred markers are synthetic oligonucleotides with unique sequences capable of amplification, e.g. by PCR. Electrophoretic markers comprising a variable-length alkyl chain and a functionalized polyhaloarene moiety are also useful. Thus, plasmid DNA encoding a fluorescent protein was incorporated into liposomes prepared from either (a) distearoylphosphatidylcholine (DSPC) 79.9 and cholesterol 20.0 weight% with 0.1 weight% distearoylphosphatidylethanolamine coupled to pentachlorophenoxypentyl 4-carboxy-2-nitrobenzyl carbonate as marker, or (b) a similar lipid composition containing dioleoylphosphatidylethanolamine (DOPE) and 6-aminomannosylcholesterol with pentachlorophenoxyhexyl 4-carboxy-2-nitrobenzyl carbonate as marker. The 2 liposome formulations were incubated simultaneously with a suspension of P1798 **tumor** cells in culture for 4 h and then subjected to fluorescence-activated cell sorting using the fluorescent protein signal to gate the collection. The homogenate of the high-fluorescence fraction of cells was irradiated at 365 nm to break the photolabile 4-carboxy-2-nitrobenzyl linker and release the electrophoretic marker, which was analyzed by electron capture gas chromatog. The predominant signal was from the pentachlorophenoxyhexyl marker, indicating that liposome formulations comprising DOPE and 6-aminomannosylcholesterol are superior to DSPC/cholesterol liposomes for delivery of plasmids into cells.

L41 ANSWER 39 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:463118 HCAPLUS
DOCUMENT NUMBER: 127:134401
TITLE: Ischemia/hypoxia-induced cell damage mediated by enhanced receptor-ligand interaction of **tumor** necrosis factor-alpha (TNF-α)
AUTHOR(S): Gerlach, H.; **Gerlach, M.**; Kerner, T.; Heid, C.; Seiler, S.; Keh, D.; Fulke, K.J.; Falke, J.
CORPORATE SOURCE: Clinic of Anaesthesiology and Critical Care Medicine, UKRV, Humboldt University, Berlin, 13353, Germany
SOURCE: Immune Consequences of Trauma, Shock and Sepsis: Mechanisms and Therapeutic Approaches, [International Congress], 3rd, Munich, Mar. 2-5, 1994 (1996), Meeting Date 1994, Volume 2, Issue Pt. 1, 412-416. Editor(s): Faist, Eugen; Baue, Arthur E.; Schildberg, F. W. Pabst Science Publishers: Lengerich, Germany. CODEN: 64SOAW
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review and discussion with 13 refs. Considering the pathophysiol. of ischemia/reperfusion-induced vascular damage, cytokine interactions with endothelial cells, elevated cytokine levels in hypoxic patients and in ischemia/reperfusion animal models, the question arose as to whether TNF-α contributes to the pathogenesis of deteriorating organ function after ischemia/reperfusion periods. Isolated human monocytes responded to varying O tensions by induction of synthesis and expression of TNF-α. Hypoxia alone induced enhanced binding of TNF-α to specific receptors on the endothelial cell surface in a time and dose-dependent manner by a mechanism not dependent on O radicals. Twelve-h hypoxia changes the affinity and number of binding sites for TNF-α on endothelial cells; however, 12-h hypoxia and 24-h reoxygenation changes affinity and decreases the number of binding sites for TNF-α. The proposed involvement of cytokine-dependent pathways in pathogenesis or organ dysfunction and multiple organ failure after hypoxia/ischemia and reoxygenation/reperfusion may be a basis for understanding initiation of hypoxic vascular injury.

L41 ANSWER 40 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:272864 HCAPLUS
DOCUMENT NUMBER: 126:342887
TITLE: Effects of dietary arachidonic acid on human immune response
AUTHOR(S): Kelley, Darshan S.; Taylor, Peter C.; Nelson, Gary J.; **Schmidt, Perla C.**; Mackey, Bruce E.; Kyle, David
CORPORATE SOURCE: USDA, ARS, Western Human Nutrition Research Center, Presidio of San Francisco, CA, 94129, USA
SOURCE: Lipids (1997), 32(4), 449-456
CODEN: LPDSAP; ISSN: 0024-4201
PUBLISHER: AOCS Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Arachidonic acid (AA) is a precursor of eicosanoids, which influence human health and the in vitro activity of immune cells. We therefore examined the effects of dietary AA on the immune response (IR) of 10 healthy men living at our metabolic suite for 130 d. All subjects were fed a basal diet containing 27 energy percentage (en%) fat, 57 en% carbohydrate, and 16 en% protein (AA, 200 mg/d) for the first and last 15 d of the study. Addnl. AA (1.5 g/d) was incorporated into the diet of six men from day 16 to 65 while the remaining four subjects continued to eat the basal diet. The diets of the two groups were crossed-over from day 66 to 115. In vitro indexes of IR were examined using the blood samples drawn on days 15, 58, 65, 108, 115, and 127. The subjects were immunized with the measles/mumps/rubella vaccine on day 35 and with the influenza vaccine on day 92. Dietary AA did not influence many indexes of IR (peripheral blood mononuclear cell **proliferation** in response to phytohemagglutinin, Con A, pokeweed, measles/mumps/rubella, and influenza vaccines prior to immunization, and natural killer cell activity). The post-immunization **proliferation** in response to influenza vaccine was about fourfold higher in the group receiving high-AA diet compared to the group receiving low-AA diet (P = 0.02). Anal. of variance of the data pooled from both groups showed that the number of circulating granulocytes was significantly (P = 0.03) more when the subjects were fed the high-AA diet than when they were fed the low-AA diet. The small increases in granulocyte count and the in vitro **proliferation** in response to influenza vaccine caused by dietary AA may not be of clin. significance. However, the lack of any adverse effects on IR indicates that supplementation with AA may be done safely when needed for other health reasons.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L41 ANSWER 41 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:263760 HCAPLUS
DOCUMENT NUMBER: 124:331640
TITLE: Fluorescence imaging studies for the disposition of daunorubicin liposomes (DaunoXome) within **tumor** tissue
AUTHOR(S): Forssen, E. A.; Male-Brune, R.; Adler-Moore, J. P.; Lee, M. J. A.; **Schmidt, P. G.**; Krasieva, T. B.; Shimizu, S.; Tromberg, B. J.
CORPORATE SOURCE: NeXstar Pharmaceuticals, Inc., San Dimas, CA, 91773, USA
SOURCE: Cancer Research (1996), 56(9), 2066-75
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Unilamellar liposomes that retain their contents in the systemic circulation can alter the pharmacokinetics of **anticancer** agents in favorable ways. It has long been recognized that certain liposome compns. will extravasate at sites of growing **tumors** and may increase the local drug concentration substantially above that achievable with a free drug. We report here that liposomes can alter the in vivo disposition of an entrapped drug not only on a macroscopic but also on a microscopic scale. We show through in vitro studies that intact liposomes composed of distearoylphosphatidylcholine and cholesterol and containing daunorubicin (DaunoXome) are taken up into P1798 **tumor** cells. These liposomes produce an enhanced cytotoxicity relative to the free drug for incubation times longer than about 8 h. For in vivo studies, we developed and used a noninvasive fluorescence imaging technique to follow the accumulation of liposomal daunorubicin within murine **tumors.** With this method, we show that the maximum concentration of the available liposomal drug in **tumors** exceeds that of the free drug, and addnl., liposomal daunorubicin persists at high levels for several days. Total liposome-delivered drug fluorescence from whole **tumor** exts. peaks at about 8 h. In comparison, the fluorescence intensity of daunorubicin released from vesicles seen with the in vivo imaging experiment peaks at 28-32 h. This apparent delay is due to a sustained release of the drug from liposomes in the **tumor.** Fluorescence microscopy of thin sections of **tumors** from animals injected i.v. with liposomal daunorubicin demonstrate persistent high levels of daunorubicin fluorescence within cells and throughout the **tumor** masses. Free daunorubicin, in contrast, transiently achieves modest levels of fluorescence and rapidly drops to background within a few h. These results indicate distinct mechanisms for the localization of free and liposomal daunorubicin, suggesting that liposomal daunorubicin can provide sustained intracellular levels of the drug within the **tumor.**

L41 ANSWER 42 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:712265 HCAPLUS
DOCUMENT NUMBER: 123:93337
TITLE: Pharmaceutical and cosmetic liposomes containing encapsulated proteins
INVENTOR(S): **Schmidt, Peter Christian**; Karau, Christine; Fleck, Monika; Walch, Hatto
PATENT ASSIGNEE(S): Dr. Rentschler Arzneimittel GmbH und Co., Germany
SOURCE: Ger., 7 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4402867	C1	19950614	DE 1994-4402867	19940131
WO 9520379	A1	19950803	WO 1995-EP175	19950118
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 740547	A1	19961106	EP 1995-906969	19950118
EP 740547	B1	19990224		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10502328	T2	19980303	JP 1995-519862	19950118

AT 176865	E	19990315	AT 1995-906969	19950118
ES 2128710	T3	19990516	ES 1995-906969	19950118
PRIORITY APPLN. INFO.:			DE 1994-4402867 A	19940131
			WO 1995-EP175 W	19950118

AB Liposomes containing encapsulated proteins, especially interferons, are prepared from phosphatidylcholine, cholesterol, phosphatidylglycerol, and α-tocopherol (6:4:1:0.01) for treatment of viral infections, **tumors**, etc. Inclusion of phosphatidylglycerol in the lipid mixture markedly improves the inclusion rate of proteins in the liposomes.

L41 ANSWER 43 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:122995 HCAPLUS
DOCUMENT NUMBER: 122:27886
TITLE: Plant defense responses of host plants with determinate nodules induced by EPS-defective exoB mutants of Bradyrhizobium japonicum
AUTHOR(S): Parniske, Martin; **Schmidt, Petra E.**; Kosch, Kerstin; Mueller, Peter
CORPORATE SOURCE: Fachbereich Biologie, Philipps-Universitaet, Marburg/Lahn, D-35043, Germany
SOURCE: Molecular Plant-Microbe Interactions (1994), 7(5), 631-8
CODEN: MPMIEL; ISSN: 0894-0282
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The symbiotic phenotype of exoB mutants ΔP5 and ΔP22 of B. japonicum 110spc4 was analyzed on the host plants Glycine max and G. soja. The extent of the symbiotic defects was host dependent. In combination with G. max, the B. japonicum exoB mutants induced the formation of effective nodules. Infection threads were found in the central nodule tissue of developing nodules, similar to wild-type infected nodules. However, in early stages of the interaction between the mutants and G. max, plant defense reactions occurred, among which phytoalexin accumulation was the earliest effect observed Later the rhizodermis was disrupted by longitudinal cracks caused by cortical cell **proliferations**, and rhizodermal strips were frequently peeled off the growing nodules. Results indicate that the intact EPS of B. japonicum is necessary for the prevention of plant defense reactions during early interaction with soybean. Combinations between G. max and B japonicum exoB mutants seemed to be impaired only transiently, since they resulted in effective nodule formation. However, enhanced concns. of chitinase within the central nodule tissue of B. japonicum exoB mutant induced G. max nodules proved the occurrence of plant defense reactions also in later steps of nodule development. On G. soja, B. japonicum exoB mutants lost their infectivity and induced the formation of white, uninfected and ineffective nodulelike structures at the base of lateral roots.

L41 ANSWER 44 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:649662 HCAPLUS
DOCUMENT NUMBER: 121:249662
TITLE: Liposomal delivery of boron to murine **tumors** for boron neutron capture therapy
AUTHOR(S): Feakes, D. A.; Shelly, K. J.; Hawthorne, M. F.; **Schmidt, P. G.**; Elstad, C. A.; Meadows, G. G.; Bauer, W. F.
CORPORATE SOURCE: University California Los Angeles, Los Angeles, CA, USA
SOURCE: Adv. Neutron Capture Ther., [Proc. Int. Symp.], 5th (1993), Meeting Date 1992, 395-8. Editor(s): Soloway,

Albert H.; Barth, Rolf F.; Carpenter, David E.
Plenum: New York, N. Y.
CODEN: 60EHAH
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The biodistribution of liposomal boron compds. in mice was studied for potential in boron neutron capture radiotherapy.

L41 ANSWER 45 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:582258 HCAPLUS
DOCUMENT NUMBER: 121:182258
TITLE: Microbiological studies on the storability of raw thick juice
AUTHOR(S): Fiedler, Birgit; **Schmidt, Peter Volker**; Kunkel, Katrin
CORPORATE SOURCE: Fachber. Lebensmitteltechnol., Humboldt-Univ. Berlin, Berlin, D-10115, Germany
SOURCE: Zuckerindustrie (Berlin, Germany) (1993), 118(11), 872-6
CODEN: ZUCKDI; ISSN: 0344-8657
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The storability of raw thick sugar beet juice is determined by the **proliferation** and metabolism of the microorganisms present in the product, which depend on the water activity (aw value), pH, and storage temperature of the juice and the number of microorganisms. As a rule, juice with an aw value >0.88 (equivalent to <67% dry substance by weight) is not storable. In storage tests of juice wit aw values >0.88, pH 9 was better than pH 6, and a temperature of 5° was better than 15-20° or 30°. Osmophilic yeasts in the juice are harmful. They can multiply and, with a starting cell population of 5 · 105/mL of juice at an aw value of 0.88, pH 9, and temperature of 15-20°, after 98 days, can cause macroscopic spoilage with foam formation. Juice with an aw value of ≤0.88, pH 9, and ≤1 · 103 microorganisms/mL (of which, ≤1 · 102 osmophilic yeasts) was storable for 300 days at 15-20°, provided that the surface was sprayed every 3 wks with 30 g/m2 of HCHO.

L41 ANSWER 46 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:250756 HCAPLUS
DOCUMENT NUMBER: 118:250756
TITLE: Model studies directed toward the boron neutron-capture therapy of **cancer**: boron delivery to murine **tumors** with liposomes
AUTHOR(S): Shelly, Kenneth; Feakes, D. A.; Hawthorne, M. Frederick; **Schmidt, Paul G.**; Krisch, Teresa A.; Bauer, William F.
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1992), 89(19), 9039-43
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The successful treatment of **cancer** by boron neutron-capture therapy (BNCT) requires the selective concentration of boron-10 within **malignant tumors.** The potential of liposomes to deliver boron-rich compds. to **tumors** has been assessed by the examination of the biodistribution of boron delivered by liposomes in **tumor**

-bearing mice. Small unilamellar vesicles with mean diams. of ≤70 nm, composed of a pure synthetic phospholipid (distearoyl phosphatidylcholine) and cholesterol, have been found to stably encapsulate high concns. of water-soluble ionic boron compds. The hydrolytically stable borane anions B10H102-, B12H11SH2-, B20H17OH4-, B20H193-, and the normal form and photoisomer of B20H182- were encapsulated in liposomes as their soluble sodium salts. The tissue concentration of boron in **tumor**-bearing mice was measured at several time points over 48 h after i.v. injection of emulsions of liposomes containing the borane anions. Although the boron compds. used do not exhibit an affinity for **tumors** and are normally rapidly cleared from the body, liposomes were observed to selectively deliver the borane anions to **tumors.** The highest **tumor** concns. achieved reached the therapeutic range (>15 μg of boron per g of **tumor**) while maintaining high **tumor**-boron/blood-boron ratios (>3). The most favorable results were obtained with the 2 isomers of B20H182-. These boron compds. have the capability to react with intracellular components after they have been deposited within **tumor** cells by the liposome, thereby preventing the borane ion from being released into blood.

L41 ANSWER 47 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:629234 HCAPLUS
DOCUMENT NUMBER: 117:229234
TITLE: Liposomal delivery of boron for BNCT
AUTHOR(S): Shelly, Kenneth; Hawthorne, M. Frederick; **Schmidt, Paul G.**
CORPORATE SOURCE: Dep. Chem. Biochem., Univ. California, Los Angeles, CA, 90024, USA
SOURCE: Prog. Neutron Capture Ther. Cancer, [Proc. Int. Symp.], 4th (1992), Meeting Date 1990, 259-64. Editor(s): Allen, Barry J.; Moore, Douglas E.; Harrington, Baiba V. Plenum: New York, N. Y. CODEN: 58COA3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The development of effective targeting strategies for the selective transport of boron to **cancer** cells has been the single most urgent problem in the area of BNCT. Successful therapy requires the site-specific delivery of relatively large amts. of boron to **tumors.** While liposomes, in general, do not concentrate specifically in **tumors**, it has been shown that certain liposomes can be made to accumulate in **tumors** in high concentration relative to normal tissue, including blood. Further, liposomes can encapsulate a wide variety of water soluble species in significant amts. These liposomes were investigated, as specific carriers of boron compds. to **cancerous** cells.

L41 ANSWER 48 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:625739 HCAPLUS
DOCUMENT NUMBER: 115:225739
TITLE: How can toxic elements (lead and titanium) be localized in histological sections by electronprobe x-ray microanalysis (EPMA)?
AUTHOR(S): Barckhaus, R. H.; **Schmidt, P. F.**
CORPORATE SOURCE: Inst. Med. Phys., Univ. Muenster, Germany
SOURCE: Progress in Histochemistry and Cytochemistry (1991), 23(1-4), 332-41
CODEN: PHCCAS; ISSN: 0079-6336

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lead inclusion bodies were frequently found in the nuclei and cytoplasm of the osteoclasts. This concentrate was reached in the osteoclast when, during bone resorption, they accumulate the lead salts previously incorporated in the bone matrix. These frequently appeared as roundish or oval structures of variable diameter (mean 0.5 μm) consisting of protruding filaments and electron-dense granules. The **tumor** cells, exhibiting longitudinal diams. between 50 and 70 μM, contain electron dense microareas near the nucleus that range in diameter from 0.8 to 2.4 μm. The highest titanium values were registered in the immediate vicinity of these electron dense compartments, where they considerably surpassed the peak value for calcium.

L41 ANSWER 49 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:443954 HCAPLUS
DOCUMENT NUMBER: 115:43954
TITLE: Titanium and **cancer** growth?
AUTHOR(S): Barckhaus, R. H.; **Schmidt, P. F.**; Hoehling, H. J.
CORPORATE SOURCE: Inst. Med. Phys., Univ. Muenster, Muenster, D-4400, Germany
SOURCE: Met. Ions Biol. Med., Proc. Int. Symp., 1st (1990), 284-8. Editor(s): Collery, Philippe. Libbey: Paris, Fr.
CODEN: 56ZJAL
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review and discussion with many refs. The occurrence of **tumors** under TiO2 dust exposure, i.m. Ti compds. and **neoplasms**, **malignant tumors** at the site of pacemaker implantation, and pigment deposition in the **tumor** cells are discussed.

L41 ANSWER 50 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:618071 HCAPLUS
DOCUMENT NUMBER: 113:218071
TITLE: Development of a suspension-emulsion system for parenteral application in animals
AUTHOR(S): **Schmidt, Peter C.**; Perschbacher, Harald; Steffens, Klaus Juergen; Kraemer, Hans P.
CORPORATE SOURCE: Dep. Pharm. Technol., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Acta Pharmaceutica Technologica (1989), 35(1), 34-7
CODEN: APTEDD; ISSN: 0340-3157
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacol. activities of a new suspension-emulsion formulation of 2 **antineoplastic** drugs and spironolactone, all 3 only very slightly soluble in water and oils, were tested in mice and rats. The active ingredients were ground in medium chain triglycerides using a wet ball milling process. The resulting suspension was incorporated in an oil-water emulsion using lecithin and cholesterol as emulsifiers and then homogenized by a high-pressure homogenization process. The particle size of this suspension-emulsion system was in the range of 1 to 2 μm with a few particles up to 7 μm. In vivo results showed an increased bioavailability of the **antineoplastic** drugs when compared with an aqueous suspension. Spironolactone was more effective after i.p. administration than after i.v. application, but did not reach the effect of K canrenoate. The formulations were all well tolerated by the animals.

L41 ANSWER 51 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:609693 HCAPLUS
DOCUMENT NUMBER: 113:209693
TITLE: Vascular permeability factor: a **tumor**-derived polypeptide that induces endothelial cell and monocyte procoagulant activity, and promotes monocyte migration
AUTHOR(S): Clauss, M.; **Gerlach, M.**; Gerlach, H.; Brett, J.; Wang, F.; Familletti, P. C.; Pan, Y. C. E.; Olander, J. V.; Connolly, D. T.; Stern, D.
CORPORATE SOURCE: Coll. Physicians Surg., Columbia Univ., New York, NY, 10032, USA
SOURCE: Journal of Experimental Medicine (1990), 172(6), 1535-46
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Systemic infusion of low concns. of **tumor** necrosis factor/cachectin (TNF) into mice that bear TNF-sensitive **tumors** leads to activation of coagulation, fibrin formation, and occlusive thrombosis exclusively within the **tumor** vascular bed. To identify mechanisms underlying the localization of this vascular procoagulant response, a **tumor**-derived polypeptide was purified to homogeneity from supernatants of murine methylcholanthrene A-induced fibrosarcomas that induces endothelial tissue factor synthesis and expression (half-maximal response at .apprx.300 pM), and augments the procoagulant response to TNF in a synergistic fashion. This **tumor**-derived polypeptide was identified as the murine homolog of vascular permeability factor (VPF) based on similar mobility on SDS-PAGE, an homologous N-terminal amino acid sequence, and recognition by a monospecific antibody to guinea pig VPF. In addition, VPF was shown to induce monocyte activation, as evidenced by expression of tissue factor. Finally, VPF was shown to induce monocyte chemotaxis across collagen membranes and endothelial cell monolayers. Thus, VPF can modulate the coagulant properties of endothelium and monocytes, and can promote monocyte migration into the **tumor** bed. This suggests one mechanism through which **tumor**-derived mediators can alter properties of the vessel wall.

L41 ANSWER 52 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:597988 HCAPLUS
DOCUMENT NUMBER: 113:197988
TITLE: Method of making liposomes with improved stability during drying
INVENTOR(S): **Schmidt, Paul Gardner**; Fujii, Gary
PATENT ASSIGNEE(S): Vestar, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9003795	A1	19900419	WO 1989-US4222	19891003
W: AU, DK, FI, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8943400	A1	19900501	AU 1989-43400	19891003
AU 612285	B2	19910704		

EP 437479	A1	19910724	EP 1989-911219	19891003
EP 437479	B1	19940622		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 04500803	T2	19920213	JP 1989-510462	19891003
JP 2792702	B2	19980903		
CA 2000219	AA	19900405	CA 1989-2000219	19891005
IL 91901	A1	19930610	IL 1989-91901	19891005
NO 9001852	A	19900801	NO 1990-1852	19900426
NO 180363	B	19961230		
NO 180363	C	19970409		
DK 9100596	A	19910404	DK 1991-596	19910404
US 5817334	A	19981006	US 1995-469156	19950606
PRIORITY APPLN. INFO.:			US 1988-253680 A	19881005
			WO 1989-US4222 A	19891003
			US 1990-534348 B1	19900605

AB Protectant prepns. for stabilizing liposomes during drying comprise liposomes in an aqueous medium, ≥1 protein, peptide, and/or oligopeptide, and ≥1 sugar. Lyophilization of liposomes made from distearoyl phosphatidylcholine and cholesterol (and optionally with trace amts. of ionophore A23187) was most successful when both a sugar (lactose and sucrose worked equally well) at 9% and a protein or peptide (gelatin and casein were best) at 2.5 mg/mL were present. Lyophilized bovine serum albumin/sugar liposomes showed lower percent injected dose recoveries while the gelatin/sugar lyophilized liposomes biodistributed as well as the unlyophilized liposome preparation Lyophilized liposome prepns. containing gelatin and lactose, tested within a few hours of reconstitution, showed good **tumor**-to-liver ratios as well as normal values for 111In loading, etc.

L41 ANSWER 53 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:3646 HCAPLUS
DOCUMENT NUMBER: 112:3646
TITLE: Liposome-encapsulated compounds for neutron capture **tumor** therapy
INVENTOR(S): Fujii, Gary; **Schmidt, Paul Gardner**; Gamble, Ronald Carl
PATENT ASSIGNEE(S): Vestar, Inc., USA
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8904176	A1	19890518	WO 1988-US3820	19881103
W: AU, DK, JP, KR, NO				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8928206	A1	19890601	AU 1989-28206	19881103
EP 386146	A1	19900912	EP 1989-900703	19881103
EP 386146	B1	19930428		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 03500888	T2	19910228	JP 1989-500512	19881103
CA 1314209	A1	19930309	CA 1988-582079	19881103
AT 88642	E	19930515	AT 1989-900703	19881103
KR 9709893	B1	19970619	KR 1989-71250	19890704
US 5328678	A	19940712	US 1992-998886	19921228
PRIORITY APPLN. INFO.:			US 1987-116764 A	19871104
			EP 1989-900703 A	19881103

WO 1988-US3820 A 19881103
US 1989-414589 B1 19890926

AB Neutron-capture **tumor** therapy agents comprise liposomes with a hyperosmotic concentration of an encapsulated compound, especially a B-containing compound, having an element with a large neutron capture cross-section and having an isotope that emits α particles when bombarded with neutrons. A method employing the above liposomes for neutron-capture therapy is also provided. B-containing liposomes were prepared from distearoylphosphatidylcholine, cholesterol, ionophore A23187, EDTA, and Na2B10H10 (250 mM) by sonication at 65° for 15 min; the liposomes (57.9 nm mean diameter) were vacuum eluted from Sephadex G-25-80 to exchange the outside solution for phosphate-buffered saline. A sample of the exchanged liposomes was then loaded with 111In3+; the EDTA-chelated 111In served as tracer, since direct measurement of B10H102- in animal tissue is impossible with known methods. EMT6 **tumor**-implanted mice were injected with the above liposomes and blood and tissue levels of radioactivity were determined At 24 h after dosing, the **tumor** level (10.3% injected dose/g) was greater than the blood level (7.8% injected dose/g), optimal for **tumor** therapy. For a **tumor** level of 10.3% injected dose/g 10B, the **tumor** concentration was calculated to be 10.2 μg 10B/g **tumor**, within the range considered necessary for successful neutron-capture therapy.

L41 ANSWER 54 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:592387 HCAPLUS
DOCUMENT NUMBER: 111:192387
TITLE: Autocrine **tumor** cell growth-inhibiting activities from human **malignant** melanoma
AUTHOR(S): Bogdahn, U.; Apfel, R.; Hahn, M.; **Gerlach, M.**; Behl, C.; Hoppe, J.; Martin, R.
CORPORATE SOURCE: Dep. Neurol., Cell Biol., Julius-Maximilians-Univ., Wuerzburg, D 8700, Fed. Rep. Ger.
SOURCE: Cancer Research (1989), 49(19), 5358-63
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Autocrine-secreted **tumor** cell growth-inhibiting activities were isolated from supernatants of a **malignant** melanoma cell line, HTZ 19-dM, established from a central nervous system melanoma metastasis. HTZ 19-dM was characterized by cyto- and immunocytochem. and karyotyping; cells were propagated in defined serum-free tissue culture medium for up to 8 mo. Supernatants were ultrafiltrated, dialyzed, lyophilized, and purified by Bio-GL P-10 gel permeation chromatog., leading to three active fraction pools, MIAI [melanoma-inhibiting activity (MIA), 2 kDa], MIAII (Mr 11,500-17,000), and MIAIII (proteins at the cutoff of Bio-Gel P-10). The growth of 19-dM cells was inhibited by 0.79 μg/mL MIAI, 0.13 μg/mL MIAII, and 16.7 μg/mL MIAIII (50% inhibitory concns.). MIAII could be further purified by reverse-phase HPLC; the main activity displayed a 50% inhibitory concentration of 0.33 μg/mL. On SDS-PAGE, one major band (mol. weight .apprx.14,000) and two minor bands (up to Mr 17,000) were identified. Macromol. synthesis was inhibited in 19-dM cells up to >99.5%; **tumor** stem cell colony formation was reduced by 99.89%; the inhibitory effect of MIAII was irreversible, nonsaturable, and partially antagonized by a serum factor (depending on purification stage). MIAII was heat stable (3 min at 100°) and trypsin labile. The effect of MIAII on allogeneic neuroectodermal **tumors** was also investigated; **proliferation** of two of three **malignant** melanomas and two of four glioblastomas was inhibited up to 85.2%; **proliferation** of a neuroblastoma cell line could be inhibited to

33.8%, whereas normal fibroblasts and low-grade gliomas were not influenced in their **proliferation.**

L41 ANSWER 55 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:22751 HCAPLUS
DOCUMENT NUMBER: 110:22751
TITLE: Effects of type of dietary fat on indexes of immune status of rabbits
AUTHOR(S): Kelley, Darshan S.; Nelson, Gary J.; Serrato, Claire M.; **Schmidt, Perla C.**; Branch, Leslie B.
CORPORATE SOURCE: West. Hum. Nutr. Res. Cent., Agric. Res. Serv., Presidio San Francisco, CA, 94129, USA
SOURCE: Journal of Nutrition (1988), 118(11), 1376-84
CODEN: JONUAI; ISSN: 0022-3166
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of dietary saturated and unsatd. fats of the n-6 and n-3 types on the immune status of male New Zealand white rabbits were compared. Four groups of rabbits were fed purified diets containing 1 of the following fats (7.6% weight/weight, 23 kcal%) for 5 mo: hydrogenated soybean oil (HSO), safflower oil (SFO), linseed oil (LSO), or menhaden oil (MHO). In vitro **proliferation** of peripheral blood lymphocytes (PBL) cultured with T-cell mitogens was significantly higher in the LSO group than in the other 3 groups, and that in the HSO group was higher than in the MHO and SFO groups which were not different from each other. **Proliferation** of PBL in response to B-cell mitogens was significantly higher in the LSO group than in the SFO and MHO groups. In vitro **proliferation** of splenocytes (SPC) from the LSO group was higher than that from the other 3 groups only when SPC were cultured with T-cell mitogens. Serum antibody levels against bovine serum albumin were significantly higher in the LSO group than in the SFO group after 2nd and 3rd immunizations. Spleen wts., number of SPC or PBL, and delayed-type hypersensitivity were not different among the 4 dietary groups. The LSO diet enhanced several indexes of immune status in rabbits.

L41 ANSWER 56 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:576368 HCAPLUS
DOCUMENT NUMBER: 109:176368
TITLE: Delivery vehicles with amphiphile-associated active ingredient, for drugs and diagnostic agents
INVENTOR(S): Eley, Crispin George Stewart; **Schmidt, Paul Gardner**; Fujii, Gary
PATENT ASSIGNEE(S): Vestar, Inc., USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 272091	A2	19880622	EP 1987-311040	19871215
EP 272091	A3	19881012		
EP 272091	B1	19930526		
EP 272091	B2	19981028		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DK 8706511	A	19880616	DK 1987-6511	19871211
DK 175531	B1	20041122		
AU 8782494	A1	19880616	AU 1987-82494	19871214

AU 608264	B2	19910328			
NO 8705194	A	19880616	NO 1987-5194		19871214
NO 171583	B	19921228			
NO 171583	C	19930407			
CA 1319614	A1	19930629	CA 1987-554194		19871214
JP 63233915	A2	19880929	JP 1987-317282		19871215
AT 89717	E	19930615	AT 1987-311040		19871215
ES 2056832	T3	19941016	ES 1987-311040		19871215
US 5320906	A	19940614	US 1991-842271		19911220
PRIORITY APPLN. INFO.:			US 1986-942093	A	19861215
			EP 1987-311040	A	19871215
			US 1989-342726	B1	19890424
			US 1991-777468	B1	19911016

AB Delivery vehicles, which are especially useful in vivo, comprise an outer biocompatible encapsulating layer, an inner amphiphilic active ingredient-associated layer, and an active ingredient. The biocompatible delivery vehicles solubilize the active ingredient for in vivo delivery, and are useful in NMR imaging (MRI) and targeted drug delivery. Magnetite was solubilized by sonication of a mixture of 5 mL of 8 mg/mL magnetite in phosphate buffer and 12 mg palmitic acid at 80 W at 66° for 15 min. The suspension was added to 104 mg 2:1 distearoylphosphatidylcholine-cholesterol lipid film and the mixture was sonicated under the same conditions. The suspension was injected into mice. Examination of excised liver, **tumor**, and spleen showed that the magnetite delivery vehicles are removed from the bloodstream over a period of hours, compared to other coated or uncoated magnetite particles which are typically eliminated from the blood in approx. 5 min. In dose dependence studies of tissue relaxation times on tissues excised 24 h after injection, **tumor** results showed that at low doses all the magnetite arriving at the **tumor** is solubilized but at higher doses the mechanism for solubilizing the particles is saturated and intact particles cause T2 relaxation enhancement. There is no significant T1 enhancement for liver and blood although T2 enhancement is observed; this is consistent with intact particles. For the spleen, the form of the dose-dependence suggests some dissoln. of particles, without saturation of the mechanism for solubilizing them.

L41 ANSWER 57 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:145190 HCAPLUS
DOCUMENT NUMBER: 108:145190
TITLE: Formation of DNA adducts and water-soluble metabolites of benzo[a]pyrene in human monocytes is genetically controlled
AUTHOR(S): Nowak, Dennis; **Schmidt-Preuss, Ute**; Joerres, Rudolf; Liebke, Frank; Ruediger, Hugo W.
CORPORATE SOURCE: Zent. Pneumol. Thoraxchir., Krankenhaus Grosshansdorf, Grosshansdorf, D-2070, Fed. Rep. Ger.
SOURCE: International Journal of Cancer (1988), 41(2), 169-73
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Formation of DNA adducts and of water-soluble metabolites was studied in monocytes of 86 1st-degree relatives of 15 families. Tests were performed with blood monocytes using 3H-labeled benzo[a]pyrene as a model procarcinogen. Variance anal. revealed significantly higher interfamilial than intrafamilial variations. Evidently, the formation of DNA adducts is genetically controlled. Therefore, the enhanced formation of benzo[a]pyrene-DNA adducts in lung **cancer** patients found in earlier studies may reflect a genetic predisposition for lung **cancer** in some patients.

L41 ANSWER 58 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:457492 HCAPLUS
DOCUMENT NUMBER: 105:57492
TITLE: Contrast agents for NMR imaging
INVENTOR(S): Gamble, Ronald Carl; **Schmidt, Paul Gardner**
PATENT ASSIGNEE(S): Vestar Research, Inc., USA
SOURCE: Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 160552	A2	19851106	EP 1985-302995	19850426
EP 160552	A3	19860820		
EP 160552	B1	19910227		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8502979	A	19851127	ZA 1985-2979	19850422
IL 74985	A1	19890331	IL 1985-74985	19850422
HU 37569	A2	19860123	HU 1985-1601	19850425
HU 194741	B	19880328		
DK 8501887	A	19851028	DK 1985-1887	19850426
DK 168853	B1	19940627		
AU 8541703	A1	19851031	AU 1985-41703	19850426
AU 585506	B2	19890622		
JP 60252429	A2	19851213	JP 1985-90744	19850426
JP 05086380	B4	19931210		
ES 542604	A1	19870116	ES 1985-542604	19850426
CA 1245553	A1	19881129	CA 1985-480146	19850426
AT 61117	E	19910315	AT 1985-302995	19850426

PRIORITY APPLN. INFO.:

US 1984-604721	A	19840427
US 1985-720954	A	19850410
EP 1985-302995	A	19850426

AB Paramagnetic ion-encapsulated phospholipid liposomes, useful as contrast agents for NMR imaging, provide enhanced target specificity, reduced toxicity, and amplified contrast enhancement. The liposomes may be formulated with cholesterol to promote vesicle stability and water exchange across the bilayer or contain a charged polymer such as poly-L-lysine to decrease toxicity and to enhance the relaxation rates. In addition, antibodies or other targeting agents can be attached to the surface to provide tissue-specific targeting. Thus, Gd3+-DTPA-encapsulated liposomes had min. toxicity in **tumor**-bearing Balb/c mice while yielding a maximum increase of 1/T1 (T1 = relaxation rate) and were tissue specific.

L41 ANSWER 59 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:64385 HCAPLUS
DOCUMENT NUMBER: 100:64385
TITLE: Localization of trace elements with a laser microprobe mass analyzer (LAMMA)
AUTHOR(S): **Schmidt, P. F.**
CORPORATE SOURCE: Inst. Med. Phys., Westfael. Wilhelms-Univ. Muenster, Muenster, 4400, Fed. Rep. Ger.
SOURCE: Spurenelem.: Grundlagen, Aetiol., Diagn., Ther. (1983), 12-24. Editor(s): Zumkley, Heinz. Thieme: Stuttgart, Fed. Rep. Ger.
CODEN: 50VKAW
DOCUMENT TYPE: Conference

LANGUAGE: German
AB Aspects are described of element determination in tissue with a LAMMA, including
instrumentation, anal. of stds., detection limits, quantification, and sample preparation Examples include Al detection in serum and erythrocytes, Pb detection in aorta, bone marrow cells, and bone matrix, and elements detection in bone **tumors.**

L41 ANSWER 60 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1977:449702 HCAPLUS
DOCUMENT NUMBER: 87:49702
TITLE: Radioimmunological determination of serum aldosterones. A new method for the localization of aldosteronism
AUTHOR(S): Hubl, Walter; **Schmidt, P. Karl Heinz**; Buechner, Manfred; Graupner, Joachim; Haussig, Klaus; Hildebrandt, Eberhard; Garten, Claus Dieter
CORPORATE SOURCE: II. Med. Klin., Bezirkskrankenhauses, Dresden-Friedrichstadt, Ger. Dem. Rep.
SOURCE: Tagungsbericht der Gesellschaft fuer Innere Medizin der Deutschen Demokratischen Republik (1977), 10, 95-6
Published in: Z. Inn. Med. Ihre Grenzgeb. 32(2)
CODEN: TGIDAU; ISSN: 0371-6910
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Plasma was mixed with the internal standard, extracted with CH2Cl2, evaporated, and
antiserum and aldosterone-3H were added and incubated at 4° overnight, adsorbed on dextran-C, and measured by scintillation counting. The method avoided preliminary chromatog. separation, required only 0.2 mL plasma, and could be used also for urine anal. Blood collection from the adrenal vein could be used to diagnose an aldosteronoma.

L41 ANSWER 61 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1969:528355 HCAPLUS
DOCUMENT NUMBER: 71:128355
TITLE: Effect of sulfur oxides in rats
AUTHOR(S): **Schmidt, Pavel**
CORPORATE SOURCE: Katedra Hyg., Prague, Czech.
SOURCE: Cesko-Slovenska Hygiena (1969), 14(4-5), 128-34
CODEN: CEHYAN; ISSN: 0009-0573
DOCUMENT TYPE: Journal
LANGUAGE: Czech
AB An exposure of rats for 6 months to an atmospheric containing 6.9 mg./m.3 and to an
atmospheric containing 7.7 mg./m.3 SO2 in an aerosol containing 2.5 mg./m.3 H2SO4
increased the values of the lymphogram and of the lymphocytic index, while the indexes of **proliferation** and differentiation of the monocytes were decreased in comparison with the controls. These changes resembled those observed in children living in industrial areas with highly polluted air. The body weight of the exposed animals decreased from the 4th month of exposure.

L41 ANSWER 62 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:421814 HCAPLUS
DOCUMENT NUMBER: 59:21814
ORIGINAL REFERENCE NO.: 59:3935g-h,3936a-e
TITLE: Pyrazolo[3,4-d]pyrimidines
INVENTOR(S): Druey, Jean; **Schmidt, Paul**; Eichenberger,

Kurt; Wilhelm, Max
PATENT ASSIGNEE(S): CIBA Ltd.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1106331		19610510	DE	
CH 371455			CH	
CH 377836			CH	
CH 392538			CH	
GB 893753			GB	
PRIORITY APPLN. INFO.:			CH	19590403

GI For diagram(s), see printed CA Issue.

AB The title compds. (Ia) were useful as coronary dilating agents, diuretics, bactericides, and **cancerstatic** compds. N1-Isopropyl-N2-benzylidenehydrazinc (8 g.) was heated with 8 g. Et ethoxymethylenecyanoacetate in 50 ml. C6H6 10 hrs. to give, after removal of the solvent, β-(N2-benzylidene-N1-isopropylhydrazino)-α-cyanoethyl acrylate (I). I (4 g.) was boiled 2 hrs. with 10N HCl-EtOH, EtOH distilled in vacuo, and the residue treated with 200 mh 2N HCl and extracted with Et2O. The aqueous layer was made alkaline with 2N NaOH and extracted with Et2O to give 1-isopropyl-3-amino-4-carbethoxy- pyrazole (II), m. 72-3° (cyclohexane). II (19.7 g.) was heated with 50 ml. HCONH2 5 hrs. at 200-10° to give 2-isopropyl-4hydroxypyrazolo[3,4-d]pyrimidine (III). III (10 g.) was treated with 15 g. P2S5 in 100 ml. C5H5N 4 hrs. at 130°, the mixture poured into 1000 ml. H2O, the brown precipitate dissolved in NaOH, treated with C, and repptd. with HCl to give 2-isopropyl-4-mercaptopyrazolo[3,4-d]pyrimidine (IV), m. 237- 9°. IV (19.4 g.) and 150 ml. N NaOH was treated by slow addition of 16 g. Me2SO4, and the mixture was stirred 30 min. at room temperature to give 2-isopropyl-4-thioxo-5-methyl-4,5-dihydropyrazolo [3,4-d]pyrimidine, which was filtered off (m. 178-80°). The aqueous alkaline filtrate was extracted with CHCl3 to give, after evaporation of the solvent, 2-isopropyl4-methylthiopyrazolo[3,4-d]pyrimidine (V), m. 78-9° (isoPr2O). V (10 g.) was treated in a sealed tube 6 hrs. with 40 ml. Me2NH at 90-100°. Excess Me2NH was evaporated and the residue treated with 10N NaOH to remove Me2NH. The oily product was extracted with CHCl3 and crystallized with iso-Pr2O to give 2-isopropyl-4-dimethylaminopyrazolo[3,4-d]pyrimidine, m. 13840°. V (8.5 g.) was treated with 80 ml. NH3 in an autoclave 20 hrs. at 95-100°. The residue was dissolved in 211 ml. N HCl, the solution filtered, and the filtrate made alkaline with 10N NaOH to precipitate 2-isopropyl-4-aminopyrazolo[3,4-d]pyrimidine, m.236 7 (EtOH- Et2O). Nt-Methyl-N2-benzylidenehydrazine (65 g.) was refluxed with 85 g. Et ethoxymethylenecyanoaeetate in 500 ml. C6H6 10 hrs. to give β-(N2-benzylidene-N1-methylhydrazino)-αcyanoethyl acrylate (VI), m. 155-6°. VI (80 g.)was refluxed 2 hrs. with 10N HCl-EtOH, EtOH evaporated in vacuo and the residue dissolved in 200 mh 2N HCl and extracted with Et2O. The aqueous layer was made alkaline with 2N NaOH and extracted with Et2O to give 1-methyl-3-amino-4-carbethoxypyrazole (VII), b0.01 130°, m. 92 3°. II (5 g.) was heated 10 hrs. with 15 ml. HCONH2 at 190° to give 2-methyl-4-hydroxypyrazolo[3,4-d]pyrimidine (VIII), m. 193° (H2O). VIII (10 g.) was treated with 80 g. P2S5 in 200 ml. C5Hs5N 6 hrs. at 115. The solvent was removed in vacuo, the residue

dissolved in 300 ml. H2O and the precipitate dissolved in 2N NaOH. Addition of 2N HCl precipitated 2 methyl-4-mercaptopyrazolo[3,4-d]pyrimidine (IX), m. above 350.
IX (10 g.) was methylated with 40 mh 2N NaOH and 9 g. Me2SO4 to give 2-methyl-4-methylthiopyrazolo[3,4-d]pyrimidine (X), m. 172-3°. X (10 g.) was boiled with 10 g. PrNH2 in 100 ml. EtOH 6 hrs. to give 2,5-dimethyl-4-mercapto4,5-dihydropyrazolo[3,4-d]pyrimidine, m. 263° 5, which was filtered off and purified by sublimation in high vacuum, The filtrate was concd, to give 2-methyl-4-propylaminopyrazolo-[3,4-d]pyrimidine,(XI),m. 133°; XI.HClm. 244 6.
1-Methyl3-amino-4-cyanopyrazole (15 g.) was treated with 10 mh HCONH2 10 hrs. at 190-200° to give 2-methyl-4-aminopyrazolo[3,4-d]pyrimidine, m. above 350° (H2O).

L41 ANSWER 63 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:81557 HCAPLUS
DOCUMENT NUMBER: 58:81557
ORIGINAL REFERENCE NO.: 58:13967g-h,13968a
TITLE: 1-Isopropylpyrazolo[3,4-d]pyrimidines
INVENTOR(S): Druey, Jean; **Schmidt, Paul**
PATENT ASSIGNEE(S): CIBA, Ltd.
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1134997		19620823	DE	
PRIORITY APPLN. INFO.:			CH	19571122

GI For diagram(s), see printed CA Issue.
AB Addition to Ger. 1,056,613 (CA 55, 13457a) The title compds. (I) which show **antitumor**, coronary dilating, and diuretic action were prepared by reaction of 1-isopropyl-4-chloro-(II) or 4,6-dichloropyrazolo[3,4-d]pyrimidine with PrNH2 (III), Pr2NH, or iso-PrNH2. Thus, 18 g. II and 50 cc. III was heated in a sealed tube at 120-30° for 5 hrs., evaporated in vacuo, the residue dissolved in CHCl3, the solution washed with N NaOH, and the CHCl3 solution distilled to yield 70% 1-isopropyl-4-propylaminopyrazolo [3,4-d] pyrimidine, b0.2 145-8°; HCl salt m. 172-3°.
Similarly prepared were the 4-isopropylamino derivative, 63% yield, m. 149-50° (HCl salt m. 188-90°), the 4-dipropylamino derivative, 81% yield, b11 195-7° (HCl salt m. 153-5°) and the 4,6-bis(propylamino) derivative of I, 65%, b0.3 178-80°.

L41 ANSWER 64 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:458857 HCAPLUS
DOCUMENT NUMBER: 57:58857
ORIGINAL REFERENCE NO.: 57:11735d-f
TITLE: Relation of isohemagglutinin levels to γ-globulin changes in disease
AUTHOR(S): Shohl, Jane; Morrison, Eleanor G.; Fahey, John L.; **Schmidt, Paul J.**
CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD
SOURCE: Journal of Laboratory and Clinical Medicine (1962), 59, 753-9
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The titers of isoagglutinin (I) (both anti-A and anti-B) were determined in the

serums of 100 patients with various diseases (named) which affected γ-globulin (II) levels. The values for I (known to be chiefly 18 S II) correlated with the total levels of II. Low I often occurred secondary to protein loss (exudative enteropathy and nephrosis) and in **malignant** disease of plasma cells and lymphocytes (multiple myeloma, Waldenstrom's macroglobulinemia, and chronic lymphocytic leukemia). In certain **malignancies** individual values frequently departed from group trends. Serums were found with normal I levels, although II values were low and vice versa. These results indicated that factors controlling I levels may differ from those controlling 6.6 S II levels. In some cases, low 6.6 S II levels may result from an increased catabolism of these proteins. 24 references.

L41 ANSWER 65 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:25149 HCAPLUS
DOCUMENT NUMBER: 56:25149
ORIGINAL REFERENCE NO.: 56:4782b-g
TITLE: 3-Aminopyrazolo[3,4-d]pyrimidines
INVENTOR(S): Druey, Jean; **Schmidt, Paul**; Eichenberger, Kurt; Wilhelm, Max
PATENT ASSIGNEE(S): C I B A Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1088503		19600908	DE	

GI For diagram(s), see printed CA Issue.

AB I(R = dialkylamino) were prepared by treating N:CR.N:CH.CR1:CR2 (II) (R = dialkylamino, R1 = cyano, R2 = Cl) with H2N-NH2.H2O (III). Thus, a mixture of 8.3 g. II (R = Me2N, R1 = CN, R2 = Cl) (IV) and 4.6 g. III in 100 cc. EtOH was refluxed 1 hr., filtered and the precipitate refluxed 1 hr. in EtOH-HCl to give I (R = Me2N) HCl salt, m. 267-9° (EtOH). I (R = piperidino), m. 281° (EtOH), was obtained by refluxing a mixture of 5 g. II (R = piperidino, R1 = CN, R2 = Cl) (V) and 10 g. III in 75 cc. EtOH 3 hrs., evaporating in vacuo, filtering the solution of the residue in 2N HCl, and precipitating with 2N NaOH. I (R = morpholino), m. 282° (EtOH), was prepared similarly. 2-Methylthio-4-hydroxy-5-cyanopyrimidine (VI) (60 g.) and 80 cc. liquid Me2NH was kept 6 hrs. at 90-100° in a sealed tube, excess Me2NH evaporated, the solution of the residue in H2O filtered, and 2N HCl added to precipitate II (R = Me2N, R' = CN, R2 = HO), which was chlorinated by keeping 13 g. with 60 cc. POCl3 2 hrs. at 110° evaporating the POCl3, pouring the residue into ice H2O, regulating to pH 8 with 2N NaOH, extracting with CHCl3, and evaporating to give IV, m. 149-150° (C6H6). V, m. 115° (C6H6-petr. ether), was prepared by refluxing 10 g. VI in 20 g. piperidine and 20 cc. EtOH 10 hrs., concentrating, and adding 2N AcOH to the solution of the residue in warm H2O to precipitate II (R = piperidino, R1 = CN, R2 = HO), m. 266° (EtOH), refluxing 10 g. in 100 cc. POCl3 2 hrs., evaporating, shaking the solution of the residue with CHCl3 with saturated NaHCO3 solution and H2O, and evaporating in vacuo. II (R = morpholino, R1 = CN, R2 = Cl), m. 170° (C6H6-petr. ether), was prepared similarly by refluxing 30 g. VI and 50 g. morpholine in 30 cc. EtOH 7 hrs., working up to give the 2-morpholino analog of VI, m. 275-6° (H2O), refluxing (25 g.) with

400 cc. POCl3, and working up. VI, m. 220-2° (EtOH), was prepd, by adding 44 g. H2NC(SMe):-NH.HI in 200 cc. MeOH to 11.2 g. KOH in 70 cc. MeOH at 0°, filtering, adding to the filtrate 33 g. EtOCH2CH(CN)CO2Et at 8-12° to precipitate Et β-(S-methylisothioureido)-α-cyanopropionate, m. 128-9°, heating (2.1 g.) in 20 cc. 0.5N NaOH 10 min. to 50°, filtering, and precipitating with N HCl. I were antimetabolites of purine, diuretics, and antirheumatics; they showed coronary-dilating and central effects. They were also efficient against infections by Ectromelia-virus and Schistosoma. They were less toxic but showed greater **tumor** -retarding response than did 4-aminopyrazolo[3,4-d]-pyrimidine.

L41 ANSWER 66 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1961:70752 HCAPLUS
DOCUMENT NUMBER: 55:70752
ORIGINAL REFERENCE NO.: 55:13457a-f
TITLE: 1-Isopropylpyrazolo[3,4-d]pyrimidines
INVENTOR(S): Druey, Jean; **Schmidt, Paul**
PATENT ASSIGNEE(S): C I B A Ltd.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1056613		19590506	DE	
CH 377834			CH	
CH 382748			CH	
CH 403785			CH	
GB 888690			GB	

AB The title compds. (I) are purine anti-metabolites and show **antitumorigenic**, coronary dilating, and diuretic action. E.g., 8.2 g. isopropylhydrazine and 16.9 g. Et ethoxymethylenecyanoacetate in 100 ml. EtOH is refluxed 12 hrs., evaporated in vacuo, and distilled in vacuo to give 2-isopropyl-3-amino-4-carbethoxypyrazole, b10 164-6°, m. 46-8°. The latter (19.7 g.) and 50 g. HCONH2 is heated in a bath at 200-10° 4 hrs., allowed to cool, dissolved in 2N NaOH, the solution treated with C, and acidified to pH 3 with HCl to give 1-isopropyl-4-hydroxypyrazolo[3,4-d]pyrimidine, m. 197-8°. The latter (7.3 g.) and 40 ml. POCl3 are refluxed 5 hrs., evaporated, the residue treated with ice water, made alkaline (pH 8) with 2N NaOH, extracted with Et2O, the extract evaporated, and the residue recrystd. from petr. ether to give 1-isopropyl-4-chloropyrazolo[3,4-d]pyrimidine (II), m. 53°. The latter (9 g.) is heated with 50 ml. NH3 at 100° 5 hrs. to give the 4-NH2 derivative, m. 152-3°. Similarly are prepared the 4-furfurylamino derivative (m. 140-1°), the 4-dimethylamino derivative, m. 69-70° (hydrochloride m. 239-41°), the diethylamino derivative (hydrochloride m. 165-70°), and the 4-methylamino derivative of I (m. 96-7°). II (9 g.) and 1.2 g. Na in 200 ml. MeOH is boiled 3 hrs. to give the 4-MeO derivative of I, m. 65-6°. II is heated with thiourea in EtOH to give the yellow 4-HS derivative of I, m. 207-8°. Ethoxymethylenemalonitrile (48.8 g.) in 500 ml. EtOH and 30 g. isopropylhydrazine is refluxed 10 hrs., evaporated in vacuo, and recrystd. from alc. to give the pyrazole, m. 94-5°. This (10 g.), 200 ml. 2N NaOH, and 100 ml. EtOH is refluxed 3 hrs., the EtOH removed in vacuo, allowed to cool, the solid filtered off, and recrystd. from EtOH to give 2-isopropyl-3-amino-4-carbamoylpyrazole, m. 215-16°. This (10 g.) and 20 g. urea are mixed well, heated in a bath at 200° 1 hr., the hot melt is added

to 150 ml. N NaOH, the mixture treated with C, filtered, made acidic (pH 3) with HCl, and the precipitate recrystd. from H2O to give 1-isopropyl-4,6-dihydroxypyrazolo[3,4-d]pyrimidine, m. 286-7° (decomposition). This is treated with POCl3 to give the 4,6-Cl2 compound (III), m. 67-8°. III (10 g.) and 70 ml. dry NH3 is heated at 100° 6 hrs. to give 1-isopropyl-4-amino-6-chloropyrazolo[3,4-d]pyrimidine, m. 260-1°. Also prepared are the 4,6-bis(dimethylamino) derivative, m. 135-6° (hydrochloride m. 206-7°), the 4,6-di-MeO derivative, m. 74-5°, the 4,6-bis(β-diethylamino) derivative (b0.2 210-25°), and the 4,6-bis(methylamino) derivative of I, m. 227-9°.

L41 ANSWER 67 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1961:65085 HCAPLUS
DOCUMENT NUMBER: 55:65085
ORIGINAL REFERENCE NO.: 55:12414i,12415a-i,12416a-c
TITLE: Structural analogs of natural purines
AUTHOR(S): **Schmidt, Paul**; Eichenberger, K.; Wilhelm, M.
CORPORATE SOURCE: Ciba Akt.-Ges., Basel, Switz.
SOURCE: Angew. Chem. (1961), 73, 15-22
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 55:65085

AB Purine analogs were prepared as possible pharmacol. active compds. or antimetabolites of nucleic acids. Derivs. of pyrazolo[3,4-d]pyrimidine (I) were prepared from either pyrimidines or pyrazoles. Thus, MeSC(:NH)NH2 and EtOCH:C(CO2Et)2 gave 2-methylthio-4-hydroxy-5-carbethoxypyrimidine, which with SOCl2 gave the 4-Cl analog (II). Similarly, 2-dimethylamino-3-amino-4-chloro-5-cyanopyrimidine (III) was prepared from EtOCH:C(CN)CO2Et (IV). With N2H4, II gave the 3-hydroxy-6-methylthio derivative of I. Condensation of IV with N-benzal- or N-acetyl-N'-alkylhydrazines, followed by hydrolysis and cyclization with alc. HCl, gave 1-alkyl-3-amino-4-carbethoxypyrazoles (V). Monosubstituted hydrazines were condensed with EtOCH:C(CN)2 (VI) or IV to give, resp., 4-cyano- (VII) or 4-carbethoxy-2-alkyl-3-aminopyrazoles (VIII). Saponification of VII gave the 4-carbamoyl derivs. (IX). VII and HCONH2 gave 1-alkyl-4-amino derivs. (X) of I. With VIII or IX, HCONH2 gave 1-alkyl-4-hydroxy derivs. (XI) of I, and (NH2)2CO gave 1-alkyl derivs. of the 4,6-dioxo-4,5,6,7-tetrahydro derivative (XII) of I. V with (NH2)2CO gave 2-alkyl-4-hydroxy derivs. (XIII) of I. Methylation of XII gave the 2,5,7-Me3 derivative (XIV), which was pharmacol. similar to caffeine. With MeNCO and NaOH, 1-methyl- (XV) or 2-methyl-3-amino-4-carbethoxy-pyrazoline (XVI) gave, resp., the 2,5-Me2 (XVII) and 1,5-Me2 derivative (XVIII) of XII. XVII and XVIII with Me2SO4 gave, resp., XIV and its 1,5,7-Me3 isomer. XVII and POCl3 gave the 2,5-dimethyl-6-chloro-4,5-dihydro derivative (XIX) of I. XIX and MeONa gave the 6-MeO analog (XX). Similarly, XVIII gave the 1,5-Me2 analogs of XIX and XX. XVI or XV with (NH2)2CS gave, resp., the 1-methyl- (XXI) or 2-methyl-4-oxo-6-mercapto-4,5-dihydro derivative (XXII) of I. With Me2SO4, XXI or XXII gave the 1,5,6-Me2(MeS) or 2,5,6-Me2(MeS) derivs., which (boiled with HCl) gave, resp., XVIII or XVII. Me2SO4 and 4-mercapto-6-oxo-6,7-dihydropyrazolo[3,4-d] pyrimidine or its 1-Me homolog gave, resp., the 2,7,4-Me2(MeS) (XXIIa) or 1,7,4-Me2(MeS) derivative (XXIII). Boiling XXIIa or XXIII with HCl gave, resp., the 2,7-Me2 or the 1,7-Me2 derivative of XII. VI and PhCH2NHNH2 gave 2-benzyl-3-amino-4-cyanopyrazole, which was saponified to the 4-carbamoyl derivative (XXIV). XXIV and (NH2)2CO gave the 1-benzyl derivative (XXV) of XII. XXV and Me2SO4 gave successively the 5-Me and the 5,7-Me2 derivative (XXVI). With H and Pd, XXVI gave the 5,7-Me2 derivative of XII (Pfleiderer and Schundehutte, CA 53 4292a. III and N2H4.H2O gave the 3-amino-6-dimethylamino derivative of I. Only the 1-isopropylamino-3-amino-6-dimethylamino derivative (XXVII) of I was isolated

from the reaction of III with Me2CHNHNH2. III and Ac-NHNHCHMe2 gave 4-(α-isopropyl-β-acetylhydrazino)-5-cyano-2-dimethylaminopyrimidine, which on boiling with HCl gave XXVII. XI and POCl3 gave good yields of the 4-Cl derivs., which with amines easily gave the 4-amino derivs. Treatment of XIII with P2S5 and then with Me2SO4 gave the 4-MeS derivs., which with amines gave the 4-amino derivs. VI and HOCH2CH2NHNH2 gave 2-(β-hydroxyethyl)-3-amino-4-cyanopyrazole, which with SOCl2 gave the β-chloroethyl derivative, which easily gave the β-aminoethyl derivs. (XXVIII) with amines. Boiling XXVIII with HCONH2 gave 1-(β-aminoethyl)-4-amino derivs. of I. With NaOH or alc. HCl, XXVIII gave, resp., the 4-carbamoyl (XXIX) or 4-carbethoxy derivative (XXX). XXIX and XXX were also prepared from IV and aminoalkylhydrazines. With HCONH2, XXIX or XXX gave the 1-(β-aminoethyl)-4-hydroxy derivs. (XXXI) of I. XXXI and SOCl2 gave the 4-Cl derivs., which with amines gave the 4-amino derivs. in good yields. The 1-phenyl-4-hydroxy-6-methyl derivative of I was prepared in good yield from MeCN, Na, and 2-phenyl-3-amino-4-carbethoxypyrazole (XXXII), but in poor yield from the 4-carbamoyl analog of XXXII and Ac2O. Heating the 1-isopropyl-4-oxo-5-(β-diethylaminoethyl)-6-methyl-4,5-dihydro derivative of I with 80% H3PO4 gave 2-isopropyl-3-aminopyrazole-4-(β-diethylaminoethyl)carboxamide. Ac2 and NH2NHCOCH2CN gave 3,4-dimethyl-5-cyano-6-pyridazinone CA 49, 2439b, 8988h, which with POCl3 gave 3,4-dimethyl-5-cyano-6-chloropyridazine (XXXIII). With N2H4, XXXIII gave 3-amino-4,5-dimethylpyrazolo[3,4-d]pyridazine. Coupling of 2-substituted-3-aminopyrazoles CA 52, 16338d, with benzenediazonium chlorides (e.g., p-ClC6H4N2Cl gave the 4-phenylazo derivs., which were reduced to 3,4-diaminopyrazoles (XXXIV). XXXIV and 1,2-dicarbonyl compds. (e.g., Ac2) gave pyrazolo[3,4-b]pyrazines Taylor, et al; CA 52, 10106g. 5-Hydroxy-3-aminopyrazole boiled with Ac2CH2 gave 3-hydroxy-4,6-dimethylpyrazolo[3,4-b]pyridine, which was also prepared from 2,4-dimethyl-5-carbethoxy-6-chloropyridine and N2H4.H2O (P. Schmidt, Kd. Meier, and J. Druey, Angew. Chemical 70, 344(1958)). Diazotization of 2-alkyl-3-amino-4-carbamoylpyrazoles gave 7-alkyl-4-oxo-3,4-dihydropyrazolo[3,4-d]-1,2,3-triazines [4-hydroxypyrazolo[3,4-d]triazines] (XXXV), which decomposed approx. 100° with gas evolution. Alkylation of XXXV easily gave the 3-alkyl derivs. (XXXVI), which were appreciably more stable. Alkaline hydrolysis of 2-methylthio-4-amino-5-cyanopyrimidine (XXXVII) gave the 5-carbamoyl derivative, which, with HCONH2, gave the 4-hydroxy-7-methylthio derivative (XXXVIII) of pyrimido[4,5-d]pyrimidine (XXXIX). With alkylamines, XXXVIII gave the 7-alkylamino derivs. (XL). XXXVII and alkylamines gave the 2-alkylamino derivs. (XLI). Alkaline hydrolysis of XLI gave the 5-carbamoyl derivative, which condensed with HCONH2 to give XL. Treatment of XL with P2S5 followed by Me2SO4 gave the 4-methylthio derivs., which (with amines) gave the 4,7-bisamino derivs. Several derivs. of I were vasodilators; the 1-isopropyl-4-diethylamino derivative had a noteworthy coronary dilatory action. Some 7-phenyl analogs of XXXVI were diuretics. X were active against adenocarcinoma and Walker carcinosarcoma. Some 4-substituted-7-dimethy]amino derivs. of XXXIX inhibited the growth of Walker carcinosarcoma and uterisepithelioma. 26 references.

L41 ANSWER 68 OF 69 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:111822 HCAPLUS
DOCUMENT NUMBER: 53:111822
ORIGINAL REFERENCE NO.: 53:20070d-i,20071a-e
TITLE: Chemotherapeutic studies in the heterocyclic series. XXVI. Pyrazolopyrimidines. 4. Aminopyrazolo [3,4-d]-pyrimidines
AUTHOR(S): **Schmidt, P.**; Eichenberger, K.; Wilhelm, M.; Druey, J.

CORPORATE SOURCE: C I B A Akt.-Ges., Basel, Switz.
SOURCE: Helvetica Chimica Acta (1959), 42, 763-72
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 53:111822

AB cf. preceding abstract Condensation of 4-chloro-5-cyanopyrimidines with hydrazines gave 3-aminopyrazolo[3,4-d]pyrimidines; 3-amino-4-carbethoxypyrazoles with HCONH2 gave 4-hydroxypyrazolo[3,4-d]pyrimidines, which were converted to the 4-halo and the 4-amino compds. Et S-methylisothioureidomethylenecyanoacetate (21 g.) and 200 ml. 0.5N NaOH heated 15 min. at 50°, filtered, and N HCl added to the filtrate to pH 1 gave 10 g. 2-methylthio-4-hydroxy-5-cyanopyrimidine (I), m. 220-3° (EtOH). Then, 16.7 g. I and 40 ml. Me2NH heated 6 hrs. at 90-100° in a sealed tube, filtered, and 2N HCl added to pH 7 gave 12 g. 2-dimethylamino-4-hydroxy-5-cyanopyrimidine (II), m. 294-96°. Treatment of 13 g. II with 60 ml. POCl3 2 hrs. at 110°, evaporation, addition to ice-H2O (and 2N NaOH to pH 8), extraction with CHCl3, evaporation, and recrystn. (C6H6) gave 12 g. 2-dimethylamino-4-chloro-5-cyanopyrimidine (III), m. 149-50°. N2H4.H2O (4.6 g.) in 100 ml. EtOH and 8.3 g. III boiled 1 hr., filtered, the crystalline product heated in alc. HCl 1 hr., and the precipitate recrystd. (EtOH) gave 7 g. 3-amino-6-dimethylamino-pyrazolo[3,4-d]pyrimidine-HCl, m. 268-70°; free base, m. 279-80°. Similarly, III with NH2NHCHMe2 gave 1-isopropyl-3-amino-6-dimethylaminopyrazolo [3,4-d] pyrimidine, m. 147-9° (petr. ether), also prepared by heating 2-dimethyl-amino-4-chloro-5-cyanopyrimidine with AcNHNHCHMe2 2 hrs. at 150-60°, adding 100 ml. H2O and NaOH to make alkaline, and extracting with CHCl3; the CHCl3 residue was heated 2 hrs. with 50 ml. N HCl, made alkaline, filtered, and recrystd. from petr. ether. A mixture of 2-isopropyl-3-amino-4-carbethoxy-pyrazole (17.9 g.) and 5 g. HCONH2 heated 4 hrs. at 200-10°, the mixture dissolved in 2N NaOH, treated with C, and precipitated with 2N HCl (to pH 3) gave 14 g. 1-isopropyl-4-hydroxypyrazolo[3,4-d]pyrimidine (IV), m. 197-8°. Heating 7.3 g. IV with 40 ml. POCl3 5 hrs., evaporating the POCl3, adding ice H2O and 2N NaOH (to pH 8), and extracting with Et2O gave 7 g. 1-isopropyl-4-chloropyrazolo[3,4-d]pyrimidine (V), m. 53° (petr. ether). V (9 g.) and 50 ml. liquid NH3 heated 5 hrs. in a sealed tube at 100°, the NH3 evaporated, and the white residue taken up in CH2Cl2 and recrystd. from cyclohexane gave 7 g. 1-isopropyl-4-aminopyrazolo[3,4-d]pyrimidine, m. 152-3°. The following 1-alkyl-4-substituted pyrazolo[3,4-d]pyrimidines were prepared similarly [1- and 4- substituents, resp., salt (if the compound is not the free base) and m.p. shown]: Et, HO, 236-7°; Et, Et2N, HCl, 170-1°; Et, PrNH, HCl, 216-18°; iso-Pr, Bu2N, b0.2 150°; iso-Pr, Et2N, HCl, 160-2°, iso-Pr, Me2N, HCl, 239-41°; iso-Pr, piperidino, HCl, 223-5°; 1-iso-Pr, morpholino, 103°; iso-Pr, MeNH, 96°; iso-Pr, EtNH, HCl, 212-14°; iso-Pr,furfurylamino, 140-1°; iso-Pr, PrNH, HCl, 172-3°; iso-Pr, iso-PrNH, HCl, 187-90°; sec-Bu, HO, 174-5°; sec-Bu, Cl, b13 137°; sec-Bu, Me2N, HCl, 228-9°; sec-Bu, iso-PrNH, HCl, 181-2°; Et2CH, HO, 142-3°; Et2CH, Cl, b11 140°; Et2CH, PrNH, HCl, m. 118-21°; Et2CH, Et2N, HCl, 167-8°; Me2CHCHMe, HO, 190-2°; Me2CHCHMe, Cl, 42-4°; Me2CHCHMe, PrNH, HCl, 150-2°; Me2CHCHMe, Et2N, HCl, 182-4°; cyclopentyl, HO, 225-5.5°; cyclopentyl, Et2N, HCl, 177-9°; cyclohexyl, HO, 245-6°; cyclohexyl, Cl, 67.5-8.5°; cyclohexyl, H2N, HCl, 236-8°; 1-cyclohexyl, EtNH, 172-2.5°. The 2-alkyl-3-amino-4-carbethoxypyrazoles prepared as before were: 2-Me, b0.05

121°; 2-Et, b0.6 121°; 2-HOCH2CH2, b0.1 186°; 2-iso-Pr, m. 61°; 2-sec-Bu, b0.09 106°; Et2CH, b11 175°; 2-Me2CHCHMe, b0.2 140°; 2-cyclopentyl, b0.15 152°, m.63-5°; 2-cyclohexyl, m. 115-16°. 1-Methyl-3-amino-4-carbethoxypyrazole (50 g.) and 200 ml. HCONH2 heated 3 hrs. at 200°, and the precipitate recrystd. (H2O) gave 20 g. 2-methyl-4-hydroxypyrazolo[3.4-d]-pyrimidine (VI), m. 293°. Refluxing 10 g. VI with 80 g. P2S5 in 200 ml. pyridine 6 hrs., evaporating in vacuo, adding 300 ml. H2O, and filtering gave a residue soluble in 2N NaOH; the 2-methyl-4-mercaptopyrazolo[3,4-d]pyrimidine (VII), precipitated with 2N HCl and sublimed in vacuo, m. above 320°. VII (100 g.) with 90 g. Me2SO4 in 40 ml. 2N NaOH heated 1 hr. gave 6.3 g. 2-methyl-4-methylthiopyrazolo[3,4-d]pyrimidine (VIII), m. 172-4° (EtOH). Refluxing 10 g. VIII and 10 g. PrNH2 in 100 ml. alc. 6 hrs., filtering, and evaporating left 2-methyl-4-propylaminopyrazolo[3,4-d]pyrimidine, with no sharp m.p. (CH2Cl2-petr. ether); hydrate, m. 130-5°; HCl salt, m. 244-7°. The following 2-isopropylpyrazolo[3,4-d]pyrimidines were prepared similarly: 4-HO, m. 229-30°; 4-HS, m. 237-9°; 4-MeS, m. 78-9°; 4-Me2N, m. 138-40°; 4-H2N, m. 236-7°. EtOCH:C(CN)2 (122 g.) in 500 ml. C6H6 treated with 134 g. MeNHN:CHPh and the precipitate, recrystd. from alc. gave 178 g. PhCH:NNMeCH:C(CN)2, m. 218°; 50 g. of this boiled 20 min. with 30 ml. concentrated HCl in 400 ml. EtOH, distilled in vacuo, and the residue washed with Et2O, dissolved in 150 ml. 10N NaOH, and extracted with CHCl3 gave 27 g. 1-methyl-3-amino-4-cyanopyrazole, m. 135-6° (CH2Cl2-petr. ether). Heating with HCONH2, as before, gave 2-methyl-4-amino-pyrazolo[3,4-d]pyrimidine, m. below 320°. Some of the compds. show diuretic and cardiac activity; others inhibit **tumor** growth.

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TITLE: The examination of the Mitscherlich procedure for the determination of the fertilizer requirements of soils
AUTHOR(S): **Gerlach, M.**; **Gunther, E.**; Seidel, C.
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AB cf. C. A. 22, 1008. The expts. carried out by the authors show that Mitscherlich cannot satisfactorily use the value of the growth factor constant and consequently the law founded on it. In the Mitscherlich equation, the total quantities of the nutrient materials used in the test must not be used, but only the part of the nutrients absorbed by the plant. The value of the growth factor constant is not constant The percent increase in yield in two expts. is only equal when, besides the material tested, other growth factors such as the basic fertilization and the water are applied in the same amts. Therefore, the use of the Mitscherlich yield tables is not generally applicable. The Mitscherlich procedure for the determination of the fertilizer requirements of the soil gives no more than a well-conducted vegetation experiment would give.

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